THE

LIVER.

LECTURES ON THE PRINCIPLES AND PRACTICE OF MEDICINE.

THE LIVER.

BY

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THE

LIVER.

INTRODUCTION.

Our knowledge of the intimate structure and action of the liver still remains in many respects vague and incomplete, and as compared with what is known of the minute anatomy and physiology of many secreting organs our information concerning this large gland is still imperfect. Not only must it be admitted that the exact arrangement and precise relation to one another of the most important structural elements have not yet been conclusively determined, but we are unable at this time to give an adequate explanation of the most important changes which occur during the healthy action of the liver. Nor is there reason to hope that our knowledge will soon be sufficiently advanced and accurate to enable us to answer many simple questions that might be proposed on the precise work discharged by the organ. In short, many broad and fundamental phenomena of hepatic action have to be further investigated. But before any such investigation can be undertaken with good prospect of success, new methods of enquiry have to be discovered, and some time must pass before we shall be able to give a clear account of the changes effected by the liver-cell.

The irreconcilable differences of opinion as to the correct interpretation and real import of facts of minute anatomy and the conflicting assertions with regard to the very first principles upon which all growth and cell action depend, cannot be attributed to any lack of interest, skill, or patient devotion on the part of highly trained investigators, but are due rather to the extreme difficulties which beset the enquiry, some of which appear to us to be even greater than any which presented themselves to our predecessors. Nay, the time when the solution of many questions may be expected seems to be caused to recede by the progress of minute research. Although of late years we have unquestionably advanced as to our means and powers of investigation—although we are able to penetrate much more deeply into the wonders of minute structure owing to improved methods of preparing tissues unknown to our predecessors, it is to be regretted that our more precise knowledge

of structural details has in many instances only served to more fully expose to our view how very little we really know, and how vast is the gulf which intervenes between our present information and that full and adequate knowledge of the arrangement and action of minute structure which can alone satisfy the mind. And, alas, by not a few of the new and improved methods of enquiry have been introduced new sources of error, and these will have to be exposed and corrected before any real advance towards the solution of important questions can be made. And, lastly, progress is unfortunately hampered by numerous authoritative but too often perfectly absurd speculations, which, though resting upon no real foundation of facts of observation or experiment, it is nevertheless most difficult to shake or refute because they are determinedly supported by an arbitrary faction which having gained power and authority, is able but too often to monopolise the interest of the ignorant and to force upon public attention any dogmas it chooses to proclaim, to the detriment of knowledge and progress, and to the injury of all real workers and work.

To determine the precise structure and relation of the several very soft and delicate structures in close apposition which constitute the liver, must be exceptionally difficult, as the slightest mechanical pressure or violence completely alters their appearance, when submitted to microscopical examination. To cut sections without previous artificial hardening is almost impossible, while all the processes of hardening which have been tried so alter the appearance and even the relation of the anatomical constituents, that it is to be feared that ideas far removed from a correct view of the structure and action have been formed, accepted, and taught, in some instances with the greatest confidence, though, nevertheless, widely differing from the truth.

In the living body the anatomical elements of the liver afford one another mutual support, but soon after death the fluid which occupies the interstices between them causes softening and other changes. A very wide departure from the natural state and appearances of the part is therefore certain. Nor is it surprising that appearances seen in different cases should have led to much difference of opinion, and to the formation of a number of hypotheses some of which are mutually incompatible.

Very many artificial methods of preparation have been adopted with the view of preventing or retarding the changes which are known to commence very soon after death and quickly result in the breaking down of the tissue. But, unfortunately, some of the methods which remedy certain difficulties create new ones, and thus any advantage derived from the process has been more than counterbalanced. Of the conclusions recently arrived at concerning the arrangement of the elements of the hepatic tissue which have been deduced from certain

special methods of preparation, some may be shown to be impossible not only as regards the liver, but in the case of any other secreting organ.

The incompleteness which characterises our knowledge of the anatomy of this important organ, and the precise relation to one another of its structural elements, unfortunately extends also to the chemical actions which occur both in health and disease. Although many important facts have been brought to light, everyone who has studied the subject must be impressed with the vagueness and improbability of many of the conclusions which are taught and which are pressed upon us with all the confidence reposed in established truth; and the thoughtful observer will soon feel obliged to confess that a great amount of new knowledge must be acquired before anything like a clear exposition of the physiological chemistry of the liver-cell or elementary part can be arrived at.

In illustration of our want of knowledge of the changes in the liver in disease, it is only necessary to call attention to the fact that the ducts which carry off the products of secretion from the cells in every part of the organ, have been almost wholly ignored in more than one of the most elaborate treatises upon Hepatic pathology. This remarkable circumstance has failed to attract the notice of those whose duty it is to review the books in question; nor does the fact seem to have been commented upon by other observers. Indeed, the particular view we may accept concerning the anatomy and physiology of the liver seems to exert little influence upon conclusions respecting its pathology, but yet if our knowledge were as exact as it ought to be we should be able to explain the several stages through which the lobule passes in its transition from a healthy to a morbid condition. Imperfect observations and inconclusive arguments of the most elementary kind, but often advanced in the most authoritative way, continually obstruct advance, and retard or interfere with thorough investigations into the nature of the changes which occur in deranged action of the liver, while as regards the exact nature of the minute changes which prepare for or lead to structural disease of the organ, we have also very much to learn.

From what observers have actually seen, and from facts revealed by the observations of others, we endeavour to picture to ourselves the actual operations as they proceed in life and even to realise the results of the complex chemical actions in the cells. That the eye will ever be able actually to see the oscillations, the separations, and combinations of the atoms as they occur during each moment of life in the living cell-laboratory is most improbable, seeing that it involves the discovery of means of demonstrating atoms which are to us minute beyond conception,—but that the physical and chemical changes actually occurring during and after the formation of biliary

matter will be gradually ascertained, and to a great extent explained to the understanding, there can be no doubt.

Of all the organs of the body the liver has probably been the most sedulously and repeatedly studied both in ancient and modern times; and during more than two centuries its anatomy has been repeatedly investigated by highly distinguished anatomists of different countries, and its action and diseases by the most famous among physiologists and physicians.

The following extracts afford evidence of the fact that as long ago as 1616, the great Harvey, as Professor of Anatomy and Surgery in the College of Physicians, in his courses of lectures and demonstrations on the general anatomy of man and animals, attached due importance to the liver. He adduces many points of anatomical interest, describes the arrangement of the large vessels, and refers to some of the uses of the bile. He knew that in certain cases both liver and spleen were much enlarged, that in others the liver was small and contracted; that jaundice was associated with obstruction of the gall duct as from a calculus, and that under these circumstances the fæces were very pale and the urine dark.

> "Jecur magis dextra x totum vnde vena umbilicalis vide conexum lieni
> W. H. Tumorem meum quartana
> Vnder the Choin tutele gratia allong up to the 7 Ribb dextra supra vnde
> difficultas respirationis Tumore Jecoris
> long the short ribbs
> vpon the stomach which it covereth
> Conexum semper diaphragmati duobus fortissimis ligamentis : vmbelicali
> venæ cavæ ramo : spinæ
> aliquando costis peritoneo Colico
> Conectitur capiti per nervos Cordi vasibus
> ventriculis et lieni per ramum splenicum." p. 17.

> "Tamen vessalius
> Vesalius in nauta absque bilis vomitione
> W. H. sed forsan quia exitus intra tunicas in Intestino
> Vse Bilis a Jecore in intestina
> Vnde obstructione Icterus et fæces Albæ
> quod aliquando flatu distenta Intestina
> vnde a colico Icterus et in
> Colico vrinæ 'inters' intensæ : quia
> facile comprimitur et obstruitur ab
> obliqua insertione
> Bilis descensu stimulat ex putricibus
> Intestinum lubricat Chilum deturbat
> feces tincturam vinde Ictero albidæ
> et vrinæ intensæ et quanto intensiores
> hæ illæ albidiores ab obstructione." p. 41.

Prelectiones Anatomiæ Universales, by William Harvey, edited, with an autotype reproduction of the original, by a Committee of the Royal College of Physicians of London. J. & A. Churchill. 1886.

Little more appears to have been done in connection with the structure of the liver till the appearance of the well-known and remarkable "*Anatomia Hepatis*" of Francis Glisson, which was published in London in the year 1654. Dr. Glisson was described by Boerhaave as "omnium anatomicorum exactissimus," and the learned author of "*The Roll of the College of Physicians*" tells us that he "was one of the first of that group of English anatomists who, incited by the great example of Harvey, pursued their inquiries into the human structure, as it were in concert, and with an ardour and success that has never been surpassed." Glisson was one of that distinguished band who first adopted the system of meeting weekly in London for the purpose of scientific investigation and reporting and recording the results. These weekly meetings gave rise to the formation of the Royal Society in the year 1660.

Two hundred years ago, Dr. Glisson gave some lectures at the College of Physicians on one of his favourite subjects; and, when we consider the nature of the questions he discussed, we cannot but admire the ardour and enthusiasm with which abstruse inquiries were pursued even in those, to us, far distant days. At the time Dr. Glisson lectured on the liver, he was more than fifty years old, and had been investigating for thirty years the structure of this organ. There is, in truth, much that we may even now try to imitate, and very much that we must admire. More especially is the manner in which many of the old anatomists worked highly commendable. They steadily and continuously for many years pursued their inquiries, and often under great difficulties. They seem to have found leisure to think as well as to work; and many spent a great portion of their lives in following out some special branch of investigation. The enthusiasm with which they recount the results of their labours shows how much they loved their work.

Modern investigation into the structure of the liver may be said to have commenced with Mr. Kiernan, who embodied the results of his valuable researches in a paper presented to the Royal Society, in 1833 ("On the Anatomy and Physiology of the Liver," by Francis Kiernan, Phil. Trans., 1833). At this time the compound microscope was so imperfect an instrument that it was but little used, and Mr. Kiernan, like his predecessors and most of his contemporaries, worked chiefly with the aid of an ordinary lens of good magnifying power. The liver-cells, the agents in the secretion of bile, and concerning which volumes will yet have to be written, were at that time scarcely known, and the precise arrangement of the capillary vessels which, however, had been injected long before by the renowned Leuwenhoek, was not satisfactorily established till some years later. The correctness of many of the general conclusions established by Mr. Kiernan,

with the very imperfect means at his disposal have been confirmed by subsequent observers, and what is very remarkable is that some of the inferences drawn by him concerning the typical structure of the liver have proved to be nearer the truth than conclusions deduced from observations made many years afterwards with the aid of better instruments and greatly improved methods of investigation than were at his disposal.

It is to be particularly noted as regards the question of the manner in which the ducts commence, that Mr. Kiernan's surmises have proved to be nearer the actual truth than some of the supposed demonstrations made thirty years and more after the publication of his memoir. Though the drawing of what he supposed to be the true arrangement is rough and scarcely amounts to more than a plan, the idea therein so clearly expressed has proved to be wonderfully near the actual fact, and the conclusion is the more remarkable when it is considered that the structure of the tissue between the ducts and the vessels had not at that time been determined; and I do not think that any observer had as yet seen any even of the tolerably small ducts which exist in great number at the circumferential part of every lobule. Certainly no one had described, with anything approaching to accuracy, ducts of a size sufficiently large to have been clearly seen with an ordinary lens. Although the capillary vessels were often well injected in those days, nothing was at that time known concerning the action of the most important and really essential and constant elements, the *cells* or *liver elementary parts*, which occupied their meshes.

During the last half century very many memoirs have been published on the anatomy of the liver. I shall not attempt to give even a short outline of the conclusions of particular observers, but it may be well to direct attention very briefly to the principal general views which have met with support.

By some the liver has been regarded as a ductless gland, and it has been even maintained that the so-called cells, the only essential and constant hepatic element, really had nothing to do with the formation of the bile, and that this secretion was produced in the terminal extremities, or rather the commencements of the finest ducts. According to this notion there is no continuity between the liver-cells and the bile ducts. The glycogenic function of the liver discharged by the liver-cells is held to be of greater importance than its bile-secreting office, which according to this view may be discharged by some small cells which it is supposed occupy the commencing portion of the ducts.

According to the observations of some anatomists the liver-cells are really outside the ducts, but nevertheless it is suggested that the cells may be concerned in the formation of bile, and the secretion when fully formed may pass through the very thin membranous wall of the finest

ducts, thus gaining access to the interior, where the only further change effected in it is inspissation, much of its watery part being gradually absorbed as the bile passes along the ducts towards its destination.

Again, another conclusion was that the finest ducts impinged upon some of the marginal cells of the lobule and that the bile directly passed from them into the open mouths of the finest terminal ducts. Concerning the precise relationship of the duct-wall to the surface of the cell, and the means by which the supposed relationship was established during development, and maintained during the various changes occurring in the gland as age advanced, and in various morbid conditions of the liver, nothing was suggested by those who advanced or supported the idea.

During the last twenty years, however, the conclusions advocated by Chrzonszczewski, Henle, and Hering, have led to the conviction on the part of a large number of distinguished anatomists and physiologists that the finest gall ducts are exceedingly minute, so very small as to form a network of capillary ducts round each individual liver-cell—the finest of such ducts being perhaps less than the one hundred thousandth of an inch in diameter. Into these it is supposed that the bile passes from the cells by permeating the very thin duct-wall, while, according to another view, these apparent intercellular ducts are really bile-receiving channels scooped out of the cells, the walls being structurally continuous with the finest ducts. But again, concerning the precise relation between these finest ducts and the cells, nothing has been advanced by those who have described this arrangement; and while some think that the membrane of the duct is applied to the wall of the cell, others consider that the duct passes into its very substance. The majority of observers, however, seems to incline to the view that perhaps the finest of the so-called gall capillaries are destitute of special membranous walls of any kind, and are more correctly regarded as narrow tubular inter-spaces between the cells, sometimes appearing as minute gutters or tubular hollows scooped out of the substance of the cell. Admitting this view, how difficult it is to understand what is the precise connection between the membranous wall of the tube and the *ever-changing* surface of the cell, and in what manner these parts were brought into relation with one another.

Concerning the way in which the supposed tubes were developed, the time of their appearance, the alterations in their relationship to the cell as it changed in volume and in its progress from the central position where it first appeared towards the circumference of the lobule, the alterations occurring in the supposed gall capillaries during the enlargement or contraction of the liver-cells—nothing has been determined or even suggested. But, is it not obvious that such a view of the arrangement of

the finest gall-ducts could not be accepted, unless the most ordinary changes of which the lobule of the liver is the seat could be accounted for in a manner not inconsistent with the acceptance of such an anatomical theory?

The enquiry as to the real structure of the human liver and the precise arrangement of the several structures of which it is composed is a most difficult one, and although many different and often incompatible views have been taught with the greatest confidence, the enquirer will find it a very difficult task to decide from a study of the most important works on the subject, what is in all probability the real structure of the liver. I would ask anyone who has studied the writings of different authorities on the anatomy of the vertebrate liver whether he feels satisfied as to the correctness of any one of the several views hitherto expounded concerning the structure and action of this important organ. I would ask whether the actual connection between the small branches of the interlobular ducts which are easily demonstrated, and the terminal so-called biliary capillaries, or minute intercellular passages has been satisfactorily made out, or if the representations of the supposed connections usually introduced in anatomical works, are copies of what has been actually seen? Has anyone yet proved how the so-called intercellular biliary capillaries are related to the cells and the changes they undergo during the periods of varying activity of the secerning process—how they are developed and what changes happen when the cells alter in volume as they frequently do. Who is satisfied with the account given of the alterations, functional and structural, which take place in them during the progress of disease, for example in ordinary cirrhosis? The above are but a few of the broad questions which must occur to any one who has thought a little on the subject; the difficulties implied seem not to have presented themselves to the minds of all who have given support to the theories referred to. Until, however, these and several other objections which naturally suggest themselves shall have been adequately explained and removed, it will not be possible to regard any of the favourite views concerning the structural arrangement of the most important anatomical constituents of the liver as conclusively determined.

Now the doctrines most generally entertained at this time and taught in most of the schools are not only open to the charge of being rather vague and inconclusive, but are not compatible with the acceptance of morphological doctrines entertained and taught by the same authorities and are even opposed to broad facts generally known. Thus Hering, a writer largely quoted, while admitting that in invertebrates, in fishes, and in reptiles the cells concerned in secretion lie within tubes of which the ducts are but the continuation, maintains with regard to the liver of mammalia and birds, that the conclusions

first advanced by Chrzonozczewski, and since adopted by anatomists generally that the ducts begin by forming very minute capillary tubes which lie amongst the cells and receive the secretion they form, are correct. In truth, Hering, and many anatomists who agree with him, would have us believe that the principles upon which the liver of a frog or a fish is constructed and acts, are totally different from those upon which that of man and other mammals and birds are formed. And this view, strange to say, has been advocated by some who, nevertheless, allow that in the general appearance and arrangement of the anatomical elements, as well as in the chemical changes taking place in the organ, the evidence of a common typical structure, arrangement, and action would be probable. The differences in structural arrangement contended for would involve developmental divergence of striking and remarkable character which ought to be demonstrable in the liver of the embryo of the animals of such different hepatic types. But in truth as regards the essential structure of the liver, we are asked by some very confident authorities to accept conclusions at variance with those general principles which are accepted by all modern anatomists and physiologists, and upon which all our ideas of morphological evolution are based. According to the conclusions to which I refer, the liver of the bird and the reptile, classes which in many respects seem to be closely allied, is constructed upon very different principles, the first possessing the very fine intercellular gall capillaries while the cells of the other lie enclosed in the cavity of membranous tubes which are continuous with the ducts. The liver then in these classes exhibits two very distinct types of structure. No forms transitional between the liver composed of wide tubes containing the secerning cells and the liver consisting of cells with intercellular and intra-cellular bile-carrying tubes of excessive tenuity have as yet been discovered, and it is scarcely possible to believe that any such actually exist. In short, in the present state of our knowledge it is not possible to defend such a view even theoretically. Whether it is fit to be accepted as a "working hypothesis" I will not decide. No case in any way analogous to the supposed difference in structure contended for between the liver of the bird and the reptile can be adduced. There is, I believe, nothing like it in all nature. The belief in typical differences between the livers of two classes of vertebrata differing not very widely from one another in other respects, is directly opposed to all that is known concerning the resemblances or differences observed in the case of other organs of the body. Compare, for example, the most divergent forms of the vertebrate kidney with which we are acquainted, and we shall not only find the clearest evidence of a general plan, but in essential points an agreement in structural arrangement and physiological action which cannot

be misunderstood, and which seems to be capable of one interpretation only. There is not to be advanced an example of the corresponding gland exhibiting in different creatures a degree of divergence in structure and action approaching that contended for in the case of the liver. The divergence referred to involves remarkable difference in the manner in which the bile must leave the cell and be carried away from the spot where it is formed in order to pass into the duct. But are not the conflicting views concerning the structure, arrangement, and meaning of these so-called gall capillaries alone sufficient to raise doubts in the mind concerning the exact nature of these supposed very fine canals, and to justify us in declining to regard the question of their existence as capillary tubes with membranous walls, and their arrangement as conclusively demonstrated? That appearances are produced by artificial injections which would be accounted for if such tubes existed is certain, but it may be fairly asked if this is the only way of accounting for the appearances in question? Again, do not the views now in favour among observers really involve fundamental differences in the development of the liver of the higher and lower vertebrata which are improbable and opposed to theories of evolution and so-called morphological laws? Are they not inconsistent with many inferences generally held to have been established as regards gland morphology?

While all will acknowledge that actual demonstration must certainly be accepted as absolute proof of a structural arrangement, no matter how far it may conflict with preconceived views or with pre-established convictions, and regardless of all theories and hypotheses whatever, however authoritative, popular, or widely accepted, it cannot be doubted that progress and truth would be terribly retarded if there was not among scientific workers a general agreement that before old conclusions, resting upon broad facts established by observation and experiment, are set aside, the new facts which seem to necessitate the acceptance of a totally different and incompatible inference should have been fully proved, and should be capable of proof and demonstration to the satisfaction of many different persons.

That the gall capillaries do not fall within the conditions just laid down I shall endeavour to show, and I may remark here that while the view of the anatomy of the liver advocated in this work is not incompatible with the appearances relied upon as proof of the existence of fine capillary gall ducts, and will indeed account for the appearances held to justify this view, the conclusion, usually accepted, that the lines of injection are due to the existence of fine capillary tubes being filled with it, does not explain, and is quite irreconcilable not only with, the facts demonstrated in specimens prepared according to the method I have advocated, but also with many conclusions resulting from broad anatomical investigations of the healthy liver, and also with certain definite

alterations of structure demonstrated in certain morbid conditions of the organ in man and animals.

The anatomical structure of the healthy human liver and the changes which this large and important organ undergoes in disease have been with me a favourite study since my student days, and had I not felt compelled to adopt a view which was not favourably received by contemporary observers, I should certainly have carried my enquiries much further many years ago. The doubt and opposition which my conclusions seemed to excite in the minds of some of those who assumed authority and exercised much influence were not encouraging to further work in the direction which I was forced by my observations to take. Moreover, some of the Fellows of the Royal Society most distinguished in this department of investigation were not at all satisfied with the views I had put forward, and while it was allowed that the specimens showed what had been represented by me in the drawings, my views so far from being supported were received with chilling neutrality and doubt, if not with positive disapproval. I was not inclined in this or indeed in any other investigation to unduly press conclusions I had arrived at, or to endeavour to persuade others that my observations or inferences were infallible. From the manner in which some observers have pressed or forced their particular conclusions upon attention, one might be led to suppose that it was the recognised duty of an investigator, if not to exaggerate, at least to make the utmost of anything new that he had made out. And yet, on the other hand, we are frequently assured by scientific authority that a very modest retiring bearing becomes an investigator, and gives him an advantage in the struggle for scientific reputation. It must, no doubt, be admitted, that in modern science, as well as in religion, considerations of a political kind, a feverish enthusiasm, real or feigned, intensity of conviction, positive assertion, prophetic assurance, play no unimportant part in the establishment of views, while the frequent use of superlatives seems to be one secret of winning converts, and supporters, and advocates, and soon provides the happy investigator with that authority which entirely supersedes further discussion, and enables him to silence all doubts and objections. It is in this way that fact, knowledge, and truth get hidden deeper and deeper under an ever accumulating heap of error, from beneath which years and years elapse before disinterment can be attempted with any prospect of success.

Views quite incompatible with the results of my own enquiries have long been freely advocated and taught, and further publication seemed not advisable. I preferred to remain in the background rather than to be opposed or ignored, and perhaps forced against one's wish to plunge into controversies with antagonists it was obviously impossible to convince, and whose assertions were sure to be thought more of than my

own. Considering the great advantage enjoyed by foreign observers in favourably impressing English scientific authorities, and, on the other hand, the very small chance of persuading English anatomists to take much interest in a question considered to be settled, it was futile to attempt to further press my views upon attention at that time. Such considerations have deterred many others from prosecuting scientific enquiries, and there is no doubt that the cause of scientific work in England has been much injured by such considerations. It is difficult to propose a full and sufficient remedy for this evil state of things. It might reasonably be supposed that it was the duty of the critic to take care that due publicity was given to the results of each scientific worker, and to insist that conclusions arrived at even by obscure observers should be fairly and clearly laid before the scientific public for consideration and discussion. But alas ! this is no easy matter, and it will probably be long before a state of things so fair and desirable in itself, and so much to the interests of science, is established.

As time passes, and scientific investigators increase in number, I dare say more generous views will prevail, and scientific authority, so incompatible with real progress, will no longer be permitted to hamper and retard investigation. In the past, narrow scientific coteries, distinguished neither for intelligence nor generosity, have acquired and wielded great power, and have frequently succeeded in preventing actual and independent workers from influencing opinion, and from occupying the position which was theirs by right of work. Many have been deterred from prosecuting various branches of scientific research, and have been deprived of the honours which ought to have been conferred upon them. The followers of science are still too few to create anything like a healthy scientific public opinion, and tact and manœuvring of a political sort are still not without influence in obtaining the general acceptance of scientific theories, or in interfering with the reception of others, in spite of conspicuous merit. For a man to get any views a little opposed to the current doctrines of the day favourably considered by his scientific contemporaries still seems to require the exercise of as much tact and worldly wisdom as might win him a seat in Parliament—but a course which for the politician desiring to improve the condition and promote the material progress of the people might be justifiable and right, would be wrong and degrading in the case of a man who was seeking to establish abstract truth in any department of natural knowledge.

As long ago as the year 1854 I wrote a memoir "On the Ultimate Arrangement of the Biliary Ducts, and on some other Points in the Anatomy of the Liver in Vertebrate Animals," which was communicated to the Royal Society by Mr. Kiernan, and was published in the "Phil. Trans." for 1855. This was soon followed by a work in which

my researches were extended, and illustrated by photographs of drawings taken by myself and printed in the Laboratory I had established in 1851 at 27, Carey Street, Lincoln's Inn Fields. In 1862 I delivered a course of eight lectures at the Royal College of Physicians, which was illustrated by many diagrams and drawings, as well as by preparations placed in hand microscopes ("How to Work with the Microscope," 4th edition). The lectures were delivered on Monday evenings at half-past eight, and the following is a syllabus of the course:—"Lecture I. February 17th, 1862. Introductory—The bearing of minute research on the progress of medicine—The liver 'cell' or 'elementary part' composed of *Bioplasm* or *Germinal Matter* and *Formed Material.* Lecture II. February 24th. The Invertebrate liver—The Vertebrate liver—General arrangement—Preparation of specimens—Portal canals—Hepatic venous canals. Lecture III. March 3rd. The Lobules of the liver—Distribution of vessels—Portal veins—Hepatic artery—Hepatic duct—Vasa aberrantia—Lymphatics—Nerves—Vessels of gall bladder. Lecture IV. March 10th. Glisson's capsule—The intimate structure of the lobule—Capillaries—Cell-containing network—The liver 'cells' of vertebrate animals. Lecture V. March 17th. On the ultimate ramifications of the ducts, and of their connexion with the cell-containing network; in mammalia, birds, reptiles, and fishes—The conclusions of previous observers. Lecture VI. March 24th. The circulation in the liver—The position of the liver as a secreting organ—The liver and kidney compared—Of congestion of the liver. Lecture VII. March 31st. Diseases of the liver—Of the formation of cysts in the liver—Of fatty liver—Deposition of fatty matter; *a*, at the circumference of the lobules, *b*, in the centre of the lobules. Lecture VIII. April 7th. Diseases of the liver—Of waxy, albuminous, or amyloid degeneration of the liver—Of the structural changes occurring in cirrhosis of the liver—Conclusion."

Twelve illustrative microscopical specimens were passed round in portable microscopes during each lecture, and many of the best of the preparations were exhibited at a soiree given by Sir Henry Acland to the members of the British Medical Association, at the Oxford meeting in the same year.

The reader will no doubt enquire how it happens that while microscopical preparations exhibiting the so-called biliary capillaries have been prepared by many, and are to be seen in every collection, and can indeed easily be prepared, specimens illustrating my own views are scarcely to be met with. The fact is very few persons of any experience in this particular branch of enquiry have seen my specimens, while the preparation of such is very difficult, and involves an amount of time that no preparer of microscopical slides could possibly give with any hope of adequate remuneration. While few things are more enjoyable than

studying specimens with well-trained observers who are interested, but who have not already committed themselves to a definite conclusion, nothing is more distasteful to an investigator than troubling a person who is not interested, with minute details and vexed questions which he is not inclined to discuss, and which perhaps are far removed from any department of research with which he is familiar.

Many years have passed since new views upon the structure of the liver or any other gland were received with the enthusiasm which used to greet and encourage research of the kind, and recently minute investigation has tended in altogether different directions. It may, nevertheless, be worth while at this time to draw attention to facts and obser vations by which inferences have been established very different from those now generally received and taught with reference to the structure and action of the liver. It will also be my endeavour to show that the careful study of important pathological changes also leads to inference quite in accordance with the views I was led to entertain on the structure of the gland in a healthy state, deduced from anatomical investigation. Some who glance over my pages will, I fear, be wearied by the multiplicity of evidence I have considered it necessary to bring forward, and may reasonably object to the many details I have adduced for the purpose of establishing general conclusions very different from those now received and taught. As, however, this book is in great part an original memoir, without having any pretensions to being a systematic treatise, I hope I may be permitted to record and discuss in my own way the facts which I think have been established in the course of my work,—and this without an effort on my part so to express myself as to gain undeserved approbation, or an attempt to please the reader with the view of escaping deserved condemnation.

It is not, in my opinion, desirable to extend the tedious records and comments of the past by examining in detail and replying to the many critical remarks which from time to time have been offered upon my work by persons who have obviously formed an incorrect view of what is to be seen by a careful examination of my specimens, and who have never for themselves investigated the structure of the liver by the methods I employed or according to the principles I had enunciated after prolonged enquiry. I propose, therefore, to briefly refer to one or two only of the criticisms which have been offered in opposition to me.

One of my friends has been so very considerate as to tell me what my specimens would have shown had they been examined by him, and one observer, Prof. Budge, of Bonn, has even placed on record a drawing altered from one of my own, with the minute ducts added, which he affirms really exist, although they were not delineated or seen by me. Now the arrangement represented in this drawing of

Budge's, besides being absurd in theory, is simply impossible in fact, and unless one looks upon his drawing as a mere joke, it certainly raises suspicions in one's mind as to the manner in which some drawings of minute structures put forward as accurate representations of nature may be evolved. With regard to the particular specimen of the liver of the pig under consideration, it is only necessary to point out that it had been carefully studied by many competent observers here, that I had myself repeatedly examined it in every possible way and with different magnifying powers, and that it had been many times passed round the lecture theatre at the Royal College of Physicians and at King's College without anyone seeing the many lateral ducts which Budge assured the world really existed in that very preparation, and without anyone suggesting a doubt as to my drawing of it not being an accurate representation of what was to be seen. It is, in short, simply impossible for anyone who sees the specimen to interpret it in the manner which Budge, who has not seen it, insists is the true interpretation.

Judging partly from specimens and partly from the tenour of remarks made by some foreign observers in reference to this enquiry, one can hardly help inferring that appearances seen in microscopical specimens considered by them sufficiently distinct to justify them in drawing in the clearest manner the particular arrangement supposed by them to exist, would not have been held by many English observers, and certainly not by myself, to be sufficiently clear and definite to justify such a course. Most of the drawings in this memoir are mere copies of what has been actually seen, and in most cases demonstrated to others. But some highly theoretical ideas, far removed from the category of facts of observation, have found expression in highly elaborate and beautiful drawings, soon to be followed by others showing different arrangements—equally elaborate and beautiful, but in some instances perfectly impossible in fact, and some very highly finished drawings of the arrangements of hepatic structure illustrating some memoirs unquestionably represent a state of things inconceivable by anyone whose imagination is controlled by even a slight knowledge of physics and chemistry.

Of our recent minute anatomy some is already dead, and the same may be said concerning not a few of our facts of morbid anatomy. Nay, much of our modern physiology is a sort of ideal physico-chemical possibility of action evolved rather from the imagination contemplating changes in the crucible, the beaker, the retort, and the test tube, the watch, and the steam-engine, than from the understanding influenced by facts and arrangements demonstrated in the living growing organism which springs from the absolutely structureless and ends in death without the possibility of resuscitation or revivification.

My great object has been to endeavour to see, as it were, the organ

at work during life, and no conclusions have been arrived at which would not bear this analysis. Those who have not well studied the minute anatomy of an organ in many members of the animal series, and who at the same time have not studied the morbid changes, or have not seen and well pondered over the various derangements and diseases which come under observation day by day, can be in a position to advance a general view concerning the structure and action of an organ with any reasonable prospect of being correct. On the other hand, the student who, without investigating for himself, endeavours to ascertain from the writings of others what is the general conclusion on the minute structure of a tissue or organ, will undoubtedly have a task of insurmountable difficulty. The differences and contradictions, the incompatible assertions as to facts and matters of observation, will cause him to invent or to despair, and he will be forced to conclude that anything like a comprehensive view concerning the action of such an organ as the liver in health, and the exact way in which its work is discharged under varying physiological and pathological conditions, is not possible at this time. As regards the liver we are terribly behind. Let anyone compare our knowledge concerning any other gland or organ of the body, for example, the kidney, lungs, heart, and even the brain, with the vague information we possess concerning the structure and action of the liver.

So numerous have been the processes of investigation, highly extolled by their respective advocates, that no wonder a student finds it very difficult to determine which to select as the plan most suitable for the investigation in which he desires to engage. Nor is it an easy matter for an observer to decide which of the methods adopted for the demonstration of the minute structure of any particular tissue or organ will give the most reliable results, or enable him to form the most accurate idea of the real arrangement of the organ during life when it is actively discharging its appointed work.

In the consideration of the method best adapted for the investigation of the structure and arrangement of the minute liver ducts, I crave the indulgence of observers of the future, and beg that those who critically study my memoir will not discard or esteem too lightly processes of investigation which in my hands have yielded important results, and which therefore I recommend, merely because this or that authority dismisses my conclusions with contempt in a few impatient and condemnatory sentences. I had hoped that the method adopted by me would have been repeated by other anatomists, but in this I have been disappointed, and now so many new processes are advocated that I fear there is little prospect of any one going over old ground at present.

The particular method of preparing specimens which after many experiments I was led to adopt, not only for the liver, but, with slight

variation in detail, for all the tissues and organs of all organisms, is undoubtedly troublesome and difficult to successfully carry out without considerable skill in practice, to be obtained only by repeated efforts. The principles upon which the process rests have been fully explained. But this plan has been followed by very few. Nor has it been regarded with favour by anatomists who have been engaged in investigations of the kind, probably in consequence of the time and trouble required to obtain the skill to carry it into practice, and without which disappointment only results from its adoption.

The principles of my method of investigation have been adequately established by careful and repeated observations upon specimens from every part of the animal kingdom, and are fully described in "How to Work with the Microscope." The details of the process and the method of carrying it out practically are given at the end of this volume. I feel confident that any careful observer who patiently works according to the directions given will obtain specimens which will fully repay him for his trouble, and which will confirm what is stated in the text and delineated in my drawings. As far as I am able to judge, the specimens I have described are not open to an interpretation different from that which I have adopted.

ANATOMICAL DESCRIPTION OF THE LIVER. ITS SITUATION AND ANATOMICAL RELATIONS. VOLUME. FORM. SPECIFIC GRAVITY. COMPOSITION. CLINICAL OBSERVATION. GENERAL STRUCTURE. CONSTANT ELEMENT.

The following general description of the broad anatomy of the liver is principally compiled from "Quain's Anatomy." Edition 1882.

Lobes of the Liver.—The Liver is divided into a larger *Right* and a smaller *Left Lobe*. On the under surface of the Right Lobe are three secondary lobes. 1. *The Spigelian;* 2. *The Caudate;* and 3. *The Quadrate lobes.* The organ presents an upper *convex* and an under *concave* surface. The thickest part of the Liver is behind and to the right; the thinnest with the sharp edge, in front and to the left.

If the Liver be hardened "*in situ*," a considerable part of its under surface, viz., a portion of the *Left Lobe* and the whole of the *Spigelian*, looks backwards, and is therefore described as a posterior surface.

Surfaces and Fissures.—*The upper surface* is convex and is covered by Peritoneum. It is exactly moulded to the under surface of the Diaphragm, the division into Right and Left Lobes being marked by the *Broad Ligament.* Upon the upper surface of the Left Lobe is to be noticed a shallow depression which corresponds to the position of the Heart which is situated above.

The under surface is concave and uneven, everywhere invested by Peritoneum, except where the Gall Bladder adheres to it, and at the *Portal Fissure*, where the lesser Omentum comes off, enclosing the vessels and ducts of the organ between its layers, and stretching to the smaller curvature of the Stomach. The under surface of the Left Lobe is moulded over the subjacent Cardiac end and part of the anterior surface of the Stomach.

The under surface of the Right Lobe is divided into two parts by the Fossa of the Gall Bladder. Of these the right is the larger, and presents two shallow depressions, that produced by the *Colon* being *in front*, and that by the Right Kidney *behind*. At the mesial border of the Renal impression is a third slightly marked depression for the Duodenum. The left or mesial of the two parts into which the under surface of the right lobe is divided by the Fossa of the Gall Bladder is known as the *Quadrate Lobe*. It is over the Pyloric end of the Stomach and the beginning of the Duodenum, and when these are distended they produce impressions upon the Quadrate Lobe.

The posterior surface which is concave over the convexity of the Vertebral Column comprehends: 1. Part of the Left Lobe in front of the Cardia, and abuts against the anterior wall of the Omental Sac; the latter forms a protuberance projecting over the lesser Curvature of the Stomach. 2. *The Spigelian Lobe and the Caudate Lobe.*—The latter prolonging the former into the Right Lobe lies directly over the Foramen of Winslow. The *Spigelian* is separated from the Left Lobe by the *Fissure of the Ductus Venosus*, and from the posterior surface of the Right Lobe by the *Fossa of the Vena Cava*. The Spigelian Lobe is opposite the tenth and eleventh Dorsal Vertebræ, but it must be borne in mind that the organ varies somewhat in position in different individuals, while as the position of the body is changed considerable modification as regards the level of the Liver with respect to a given Vertebra will occur. 3. A strip of the Right Lobe, two and a half to three inches broad, which at its lower and mesial corner presents an impression for the *Right Supra-renal Capsule*. In consequence of the separation of the layers of the *Coronary Ligament*, this part is not covered by Peritoneum except at its right end.

The Transverse Fissure lies between the *Quadrate* and the *Spigelian* Lobes. It runs transversely, and the great vessels and nerves enter the organ at this spot, while the *Hepatic Duct* leaves the liver to pursue its course after the *Cystic Duct* has joined it towards the Duodenum. *The Longitudinal Fissure* between the *Right* and *Left* Lobes is divided into two parts by the Transverse Fissure. The Anterior or Umbilical Fissure contains the remnant of the Fœtal Umbilical Vein, called the Round Ligament. The Posterior is named *Fissure of the Ductus Venosus*. It is between the Spigelian and Left Lobes, and lodges

the Ductus Venosus in the Fœtus, and in the adult its remains, a slender fibrous cord.

The Fissure of the Vena Cava is at the back of the Liver, between the Spigelian and Right Lobes, and is separated from the Transverse Fissure by the *Caudate Lobe.*

Ligaments.—With one exception, the *Round Ligament*, the so-called *Ligaments* of the Liver are reflections of serous membrane. The *Coronary Ligament* is a reflection of Peritoneum round a triangular space on the posterior surface of the Liver, where it is immediately adherent to the Diaphragm. These reflections are continued on either side, and are here named *Right* and *Left* Lateral Ligaments, of which the left is the longer. *The Broad, Falciform, or Suspensory Ligament* is a wide thin membrane composed of two layers of Peritoneum, which are continuous behind with those of the Coronary Ligament. By one margin it is continuous with the under surface of the Diaphragm, and with the sheath of the Right Rectus Muscle as far as the Umbilicus. By another it is attached along the convex surface of the Liver from its posterior border to the notch on its anterior border. The remaining margin of the Falciform Ligament is free, and contains between its layers the Round Ligament, a Fibrous Cord, the remains of the Fœtal Umbilical Vein, which ascends from the Umbilicus to enter the Longitudinal Fissure.

Position of the Liver in the Body.—The organ is situated in the Right Hypochondriac region, and extends obliquely upwards across the Epigastric, to the Left Hypochondriac region, the greater part of which it occupies; the upper surface of the Liver corresponds to the vault of the Diaphragm, and is in close apposition with the under surface of this large thin muscle. In front, in the Sub-costal Angle, a small portion of the Liver comes into contact with the abdominal wall. The Diaphragm separates the Liver from the concave base of the Right Lung, the thin margin of which intervenes anteriorly between the surface of the Body and the Liver. The Convex Surface is protected on the right by the ribs from the seventh to the eleventh; in front by the cartilages of the ribs from the sixth to the ninth, and by the Ensiform Appendix, the Diaphragm being interposed.

The position of the Liver varies somewhat according to the posture. The whole organ rises and falls in the movements of respiration. In the upright or sitting posture it descends to a point just below the lateral margin of the Thorax; but in the recumbent position it ascends, and in many individuals it is for a time entirely covered by the ribs except in the Sub-costal Angle. During a deep inspiration, however, the Liver is forced downwards below the margin of the ribs in whatever posture the patient may be placed. During the ordinary respiration the Liver may rise and fall as much as two inches vertically, and in some

individuals the change in position between full inspiration and forced expiration is still greater.

Relatively as well as absolutely the Liver receives an enormous blood supply, the greater part of which is *venous*, for before it reaches the Liver the blood has already passed through the very extensive capillary system of the mucous membrane of the Stomach, the small and great part of the Large Intestine, as well as the vessels of the Pancreas and Spleen. With this venous blood, however, is intermingled in the capillary network of the Lobule of the Liver a certain proportion of arterial blood brought to it by arterioles of the Hepatic Artery.

The whole of the blood transmitted to each lobule, after having traversed the extensive capillary system, is carried away by the intra-lobular branch of the Hepatic Vein, whence it finds its way into the larger branches which at length unite to form the Hepatic Veins which open into the Inferior Vena Cava, from which the blood very quickly passes into the Right Auricle.

The Hepatic Artery, the Portal Vein, and the Bile Duct, ascend to the transverse fissure between the layers of the Gastro-Hepatic or Small Omentum in front of the Foramen of Winslow. In this course the Bile Duct is to the right, the Hepatic Artery to the left, and the large Portal Vein, between and somewhat behind both. They are accompanied by the Lymphatics and Nerves. These vessels and the branches into which they divide as they pass into the substance of the Liver are accompanied by Connective Tissue, which is irregularly distributed about them, and which seems to keep the branches in position as they ramify in the canals and fissures through which they pass to the Lobules in every part of the Liver.

The Portal Vein conveys by far the greater part of the blood which is to pass through the Liver. This vessel is formed by the union of veins from the Stomach, Intestines, Pancreas, and Spleen. It enters the Liver by the Transverse Fissure where the vessel divides into two large branches which pass into the Liver.

The Hepatic Veins, which convey the blood away from the Liver, leave the organ at its posterior border, where they form a large Sinus receiving two or three large branches and several small ones.

The Hepatic Artery is a branch of the *Cœliac Axis*, and is a very small vessel considering the large size of the organ to which it is distributed. If compared with the branch of the artery distributed to other organs and textures far inferior to the Liver in size, the Hepatic Artery will be found very small.

The vessel enters with the Portal Vein at the Transverse Fissure, and soon divides into branches which are distributed to the coats of the large veins, to the Gall Bladder and Ducts, as well as to the proper structure of each Hepatic Lobule, and to the large "Capsule" of the

Liver as well as to the coats of the smaller vessels and duct, and to the Connective Tissue called "Glisson's Capsule," which is found in all the Portal Canals and Interlobular Fissures. This Connective Tissue is present in much larger amount in the Liver of the adult and of old age than in that of infancy and childhood, and in the Liver of large animals it is more abundant than in that of small ones.

The Hepatic Duct formed by the union of a branch from the Right and Left Ducts, passes out at the Transverse Fissure, runs between the layers of the small Omentum for about two inches, and then joins the Cystic Duct at an acute angle. Thus is formed the Common Bile Duct, the *Ductus Communis Choledochus.*

The Lymphatics of the Liver form a superficial and deep set. The superficial forms a sub-Peritoneal plexus of vessels, which communicate by branches running through the Ligaments of the Liver with the Thoracic Lymphatics. The deep set of Lymphatics accompanies the Hepatic Artery and Portal Vein, and carries the lymph from a very extensive network of small Lymphatics in the Areolar Tissue which is regarded as an extension of the so-called Glisson's Capsule into the Portal Canals.

The Nerves of the Liver are derived from the Cœliac Plexus of the Sympathetic and from the *Pneumogastric Nerves*, especially the left one, some of the filaments of which form a Plexus, from which branches proceed to the Liver.

The Gall Bladder is a membranous Sac from three to four inches long, and about one and a half inches in diameter in its widest part. It is capable of containing from eight to twelve fluid ounces. It is lodged obliquely in the Fossa of the Gall Bladder on the under surface of the Right Lobe of the Liver, its large end or fundus being directed forwards, downwards, and to the right. Its under surface and fundus are covered by Peritoneum. The Gall Bladder rests below on the commencement of the Transverse Colon, the Duodenum and Pyloric end of the Stomach. The narrow end or neck bends downwards to the left, and gradually contracts to form the Cystic Duct.

DIMENSIONS—WEIGHT—ALTERATIONS IN VOLUME AND IN FORM—SPECIFIC GRAVITY—CHEMICAL COMPOSITION.

The healthy liver of a person of average size measures about twelve inches from side to side, and six or seven from front to back. It is about three and a half inches in depth in its thickest part. In bulk the healthy liver corresponds to about 100 cubic inches.

In small healthy persons the liver may weigh less than two pounds

while in tall, well-developed, active men it may exceed five pounds in weight, without exhibiting any evidence of morbid change.

It is well to note here that the relation between the weight of the liver and the total weight of the body is not the same in man and animals. As in the case of the brain, but in still greater degree, the relation of the liver to the body-weight is very different in different animals. Generally it will be found that the weight of the liver like that of the brain relatively to the body-weight is greater in small than in large animals—in those which consume large quantities of food in proportion to their size than in those which require little for their sustenance. In all, the proportion between the liver and the total body-weight is greater in intrauterine life and during the early period of existence than when the tissues and organs are fully formed, or in adult life; while in all animals, as age advances, the liver shrinks in size, as much less work is required of it.

Relatively to the body-weight, the liver also exhibits changes as the body grows, being in the infant in the proportion of one to twenty-five, while in the adult it is as one to thirty-five, and in old age as one to forty-five or fifty.

In disease the variation relatively to the body-weight is sometimes very considerable. In one direction it may become as one to eighty, while in the other it may approximate to one to seven or eight, for, as is well known, extreme general emaciation is not unfrequently associated with extraordinary enlargement of the liver.

As age advances the liver diminishes in size absolutely as well as relatively in proportion to the reduced body-weight. The most remarkable period of hepatic action, when the liver attains its largest size and its highest activity, is when the largest amount of food is assimilated, and, as ought invariably to follow, the greatest degree of tissue-activity and body-work is reached, and as a consequence the largest proportions of excrementitious matters are formed. In old age all activities are reduced. We live more quietly and more slowly, with greater economy of sustenance and less expenditure as regards the organs engaged in the change of energy, and the development of locomotor work. The activity of the working of the higher parts of our nervous system, being less dependent upon nutritive changes and food than that of other organs, continue and may even increase for some time after many glandular organs have passed their prime, or have reached a period of very reduced action, and have greatly deteriorated in structure.

The spleen excepted, there is no organ in the body which in health undergoes such considerable alteration in bulk as the liver. This depends upon the varying quantity of blood in the vessels. It is probable that when the capillaries are fully distended, the liver contains from three to four times as much blood as when the blood is reduced to

its smallest amount. In some of the lower animals the variations in bulk at different times are far greater than in the human subject, and in some there exists a special arrangement to facilitate the necessary alterations in position of the lobules with respect to one another when the organ is enlarged.

Anything that interferes with the free flow of blood through the lungs may give rise to accumulation of blood in the liver and spleen. There will be decided slowing of the circulation through the hepatic capillaries, and sometimes probably the blood stagnates in some places. Generally, in violent exercise, and more especially in swimming and diving, does the liver become distended with blood, and in some animals, notably in the seal, the short trunk of the hepatic vein is dilated so as to form an enormous sinus which receives great quantities of blood,—not only that which flows through the liver from the intestinal veins, but much that is passing from the inferior cava, and which is prevented for the time from traversing the capillaries of the lungs. In the smaller branches of the hepatic veins of this animal, as I showed in my paper in the "Phil. Trans.," is a very remarkable arrangement for the prevention of the backward pressure of the blood being transmitted to the capillaries of the lobules (page 58).

In animals that are accustomed to gorge, the circulation could not be relieved by the accumulation of blood in the hepatic vein, if that vessel were no larger in proportion than it is in man. The relief of undue pressure is attained, and at the same time other exigencies are provided for by a different arrangement. In such animals provision exists in the liver itself for the effectual prevention of damage to the secreting structure by undue congestion of the vessels. Each lobule is separated from its neighbours by much lax connective tissue, so that the veins and lymphatic vessels in the interlobular spaces become freely distended without any undue pressure being exerted upon the secreting structures of the several lobules, which move evenly upon one another, while the whole organ increases in size—not a lobule suffering from pressure, or any of its vessels from pressure or stretching.

Variations in the form of the Liver.—The variation in form as well as in size of the liver in different diseases is most striking, and to this there is no parallel in the case of any other organ in the body. Unusual growth at an early period of development of one part and defective growth in another part of the liver, may affect the gland so as to lead to unusual enlargement or reduction in size of a particular lobe or other part of the organ. Occasionally the left lobe of the liver is so much larger than the right, that when the body is examined it might be inferred that the liver was on the wrong side, which arrangement is indeed sometimes found to exist. One lobe may grow very large, and from the left in some cases pendulous portions may grow and project

downwards, and may be mistaken for cancerous or other abnormal growths. A portion of the posterior part of the left lobe has occasionally grown in such a manner as to form an elongated mass, which occupied the posterior portion of the abdominal cavity, and during life had been mistaken for a movable left kidney. From time to time other and more curious departures from the ordinary form of the lobes are met with. Upon the whole the greatest variety in the shape of the several lobes and in the form of the liver occur without disturbance of function.

Specific Gravity and Chemical Composition of the Liver.—The specific gravity of the liver is about 1050, but from what has been already stated, it must be obvious that great changes occur even in health from time to time as regards its specific gravity, which will be altered by the varying quantity and varying density of the fluids in its vessels and permeating its substance. In disease the specific gravity is generally lower than in the healthy state, and in some conditions, and particularly in fatty liver, it falls much below the usual standard ; and in extreme cases of fatty degeneration, the specific gravity of the liver may be reduced to 1030 or even lower.

The following is an analysis of a liver presumed to be healthy. The organ was taken from the body of a man thirty-one years of age, who was killed by falling from a second-floor window while in the enjoyment of good health :—

		Per 100 of Solid Matter.
Water	68·58	
Solid matter	31·42	
Fatty matter	3·82	12·16
Albumen	4·67	14·86
Extractive matter	5·40	17·18
Alkaline salts	1·17	3·72
Vessels, &c., insoluble in water ...	16·03	51·01
Earthy salts	0·33	1·05
	100·00	

It is not possible to separate entirely the secreting cells of the liver from the vessels, but the "fatty matter" and the greater part of the "albumen" and "extractive matters" in the above analysis are probably derived from the cells.

In disease, the proportion of the constituents undergoes great variation. In fatty degeneration an enormous amount of fatty matter may accumulate in the liver. In one remarkable case, I obtained as much as 75·07 per cent. of solid matter, and of this 65·19 consisted of fat. In "amyloid" degeneration the albuminous materials and the water

are increased, while the fatty matter is considerably diminished in amount.

In cirrhosis the soluble constituents of the hepatic tissue are in great part removed, and the organ is defective as regards the quantity of fat, and much of the "albuminous matter" present in health disappears.

CLINICAL.

The Liver very Sensitive to Slight Disturbance.—Of all the organs of the body the liver in its healthy state is the one which is not only most easily deranged, but the one the derangement of which more than of any other reacts upon and disturbs the action of other organs, particularly the stomach and intestines. At the same time there is no doubt that extreme sensitiveness of liver, however disagreeable to its owner, is of advantage to his organism, for what he may do and may not do with his body and mind is decided by his liver rather than by his inclination or will. Thus mental and bodily work are regulated and are kept within the limits of capacity for healthy action, and organs which would quickly suffer if subjected to strain are kept within the range of reasonable use and activity, and are preserved in working order for years, and possibly by the moderate exercise to which they are subjected actually improve in working capacity as time goes on. The long life of fidgetty dyspeptics is proverbial. They complain and grumble, and often feel as if they "did not care to live," but nevertheless they do manage to live and often to a good old age. Those dyspeptics who don't allow themselves to be made, and to make those about them wretched, often do a marvellous life's work, notwithstanding frequent breaks-down in health. In their successes as well as their sufferings and disappointments the hypersensitive liver has played no unimportant part. By itself becoming deranged, derangement or even disease of important organs has perhaps been prevented, and possibly the integrity and free action of highly important tissues of the body, the free action of which is essential to longevity, has been thus preserved far into old age. The healthy liver will rebel if too much food, and in many cases, if the wrong kind of food, be taken into the stomach, if food be swallowed too quickly, or if food of objectionable quality be introduced, if too much or too little, or the wrong kind of liquid be taken with or between the meals, if the person take too much or too little exercise, if he be over anxious about anything, if he overwork his mind, or if he is very idle, if he sleeps too much, or takes too little rest.

In many persons the proper free action of the liver seems to be the exception, and it is not uncommon to find the digestion terribly

disturbed for some weeks at a time, the motions being pale and scanty for many days in succession, while occasional periods of obstinate constipation add to the discomfort. In many such cases the patient sometimes seems to be on the eve of an attack of jaundice, but the liver usually resumes its action without the conjunctivæ being more than very faintly tinged, and may continue work properly for many days or weeks without being again disturbed. Malaise, a sense of fulness on the right side, indigestion, headache, impaired appetite, and actual distaste for food, pain in the back or in the right shoulder, are symptoms by which the patient is often informed that his liver is out of order, or does not act as freely as it ought to do.

Of Judging of the Size of the Liver by External Examination.— Perhaps there is no one fact to be determined by the physical examination of a patient concerning which such diametrically opposite conclusions are deduced as the size of the liver. One physician positively affirms that the organ is enlarged, while another as positively declares it to be smaller than natural, and possibly a third considers it to be of the normal size.

He who accepts the arbitrary statements in many books concerning the position and dimensions of the liver will be frequently led into mistakes on this point. I have seen persons whose livers were perfectly normal, who had no hepatic dulness whatever, while in others the extent of the hepatic dulness was so great as to lead to the inference that the liver was very large, although there was no conclusive reason for supposing that the organ was above the normal size. The physician must take notice of the build as well as the stature of his patient, noting particularly the length and breadth and depth of his chest, and he ought to endeavour by careful palpation and percussion to form an estimate of the size of the organ.

The area occupied by the liver may generally be made out with a near approach to correctness by careful percussion only, but the physician must not allow himself to refine too much, for a varying extent of the upper surface of the organ is covered by the lower margin of the right lung, and a much greater extent of liver is in contact with the anterior surface of the abdominal wall in some cases than in others, and an erroneous inference may be drawn if the extent of the dulness only is noted. Generally, the anterior edge of the liver in health corresponds to the lower margin of the ribs, but in some cases it seems to be half-an-inch or an inch below this line, and in others may be more than as much above. In the erect posture, and especially when the lungs are expanded by inspiration, the liver will be forced down to a lower level than it will be found to occupy when the patient is recumbent. and if while lying down he makes a forced expiration, the position of the liver, as indicated by percussion, will be found much

higher than would have been often expected. The student should carefully observe the variations in position of the liver in healthy persons as shown by the change of the limits of dull percussion in different individuals, for these are very considerable, and the matter is one in which a mistake is easily made.

Occasionally the left lobe of the liver is discovered to be exceptionally large, as large or even larger than the right lobe, and in a few rare instances the liver like the spleen and the heart will be found transposed to the side of the body opposite to that on which it is ordinarily situated. In such cases the observer who percusses over the usual situation, and finds no dulness, must not too hastily assume that the liver is excessively small or entirely absent, for the organ may really be of the usual size and perfectly healthy, though upon the opposite side of the body.

The practitioner must bear in mind that he will occasionally meet with persons in whom the liver dulness is much reduced in extent, or is even completely absent. Just as there are individuals with lungs, heart, brain, and other organs remarkably small in proportion to the body, so we find congenitally small livers. In the case of patients suffering from certain symptoms attributable to hepatic derangement or disease, this may be a source of considerable perplexity, and when the malady is jaundice, a very small liver may cause anxiety to the physician, who will fear that the case is possibly one of that rare forms of disease known as *Acute Yellow Atrophy* of the liver, which, unhappily, from time to time comes under our notice. If, as in the case of a young woman I was attending in 1885, there should be great prostration with sickness, quick pulse, and fever, the difficulty of arriving at a correct decision is greatly increased. In the case in question these latter symptoms turned out to be due only to temporary disturbance, and the patient soon got quite well, the liver still remaining exceptionally small. When it is borne in mind that in some instances the question for decision is, in fact, whether the illness is comparatively unimportant in its nature or necessarily fatal, the reader will be able to form an estimate of the anxiety experienced by the practitioner in some of these cases. Moreover, although in the majority it is certainly possible to decide as to the nature of the case at an early period, I have met with two or three instances in which one could not feel at all sure for several days whether the patient was really suffering from a serious malady, or from ordinary temporary jaundice, from which complete recovery without any structural change whatever was almost a certainty. It requires careful consideration on the part of the physician to decide whether or not he shall give utterance to the doubt he feels, for while it is of course right to inform the friends of the serious nature of a malady as early as possible, it is almost cruel even to hint at the

possibility of the patient being the subject of so very serious a disease as the one referred to, unless one feels practically convinced that this is the case.

In tall slim persons the liver is of greater depth than in those who are short and broad, and the dulness from above downwards will be an inch or two more, though the weight of the liver may be the same or nearly so in the two cases. In examining people with unusually long trunks, I have known a student to mistake the position of the liver, and fix the position of the ensiform appendix as much as four inches lower than its real place.

Although generally the amount of hepatic tissue bears a definite relation to the body-weight of the individual, not only do we find in practice great variation in size, irrespective of the body-weight recorded, but the relative weight may vary considerably at different periods of life. At one time the liver may be "large," and a few years later it may be found "smaller" than it should be, although no serious derangement of the health or of any of the physiological functions may have been induced, and even without any corresponding change in the body-weight. In those who have gradually acquired the vicious habit of eating much more food than the system requires for work and nutrition, the liver will possibly grow considerably in size. If the change is very gradually brought about, and the liver was healthy to begin with, I believe the organ may be induced to discharge much more than its proper amount of work without suffering in structure. Not un frequently we see persons who have acquired the habit of digesting perhaps twice or even three times the weight of food necessary for their bodily wants, who, possibly from being the possessors of exceptionally powerful and vigorous organs, nevertheless live to be old ; but it is quite certain that the majority who indulge in over-eating suffer from disease before the age of sixty is reached. A City dinner provides the physiological physician with abundant food for reflection, and if he could obtain the life history of the most famous of the diners he would probably have only too convincing evidence of the injury to the health resulting from continual over-feeding. For one success in inducing the liver to habitually discharge an undue amount of work, there will be a multitude of lamentable failures, persons in whom organic disease is induced, and the duration of life is very much shortened. To persuade some people to take only the quantity of food that is good for their organs is, however, in these days almost impossible, especially where they have taken for a long while the opposite direction, and have acquired the habit of over-feeding. Feeling "weak," if they reduce the intake, and fearing they will become weaker, they are led to persist in increasing the supplies till every organ is so clogged with excrementitious matters that it can no longer discharge its functions. The whole

body soon gets out of order, and for restoration long rest will be required, especially as regards those organs which rest only during "starvation," and can only properly discharge their work when but a small amount of food at a time is submitted to their action, and this system is persisted in for many months. The liver then is capable of considerable increase in size as well as reduction, not only before its development is complete, but in the adult according to the amount of work it is called upon to discharge. If, for example, a man lives very freely for a certain number of years, his liver will enlarge, while, if during a like period of time he very much reduces the quantity of food he takes, diminution of the liver will accompany the change in living, if he be generally in a healthy state. In many cases, improved general nutrition, and the converse, that is loss in nutrition, are accompanied by corresponding changes in the volume of the liver. These changes in volume are not generally uniform, but affect one part to a much greater extent than another, so that a liver which has once been enlarged seldom becomes reduced without much alteration in form. I believe increase and diminution within the healthy range often occurs several times in the course of life. New hepatic tissue and probably new lobules are formed when the organ is called upon to discharge an increased amount of work. To what age this capacity for new growth extends it is impossible to say, but there is good reason to think that in healthy persons over forty, and I think even fifty years of age, the liver may enlarge considerably, but within healthy limits, and undergo reduction in volume.

I doubt whether the relative size of the liver in proportion to the body is of so much significance in estimating the probable value of a life as the state of and size of the heart, the pulmonary capacity and free action of the lungs, the chest mobility, and a healthy condition of the kidneys; and although there is no doubt that in endeavouring to form a judgment, the probable size of the liver ought to be taken into account, unless there is very decided departure from the normal condition it is not well to lay much stress upon supposed slight modifications only in the size of the organ.

Large livers and small livers are both objectionable from a physiological point of view, and change in either direction may occasion very serious damage to the health and shorten life. Enlargement and diminution in volume may occur in the course of long continued pathological change, but generally while it is common for an enlarged liver to become reduced in size, I have never known a contracted liver to regain its normal dimensions.

The liver is an organ that readily adapts itself to the shape of the cavity in which it lies, and to that of the organs with which it is in contact. If the parietes encroach upon any part of its surface, this soft gland seems to yield, or perhaps it would be more correct to say that

the gland structure grows in adjacent situations where there is no pressure, or where the pressure exerted is least severe.

Surface of the Liver.—The part of the anterior surface of the liver enlarged by disease projecting below the ribs and felt through the abdominal walls may be uniformly smooth, or there may be irregularities or inequalities of surface varying greatly in dimensions and in the degree they extend from the general surface. The edge of the liver may be felt easily enough in some persons, and the notch corresponding to the gall bladder may be distinctly traced. In many cases of enlargement the edge is rounded and sometimes it is very irregular. Where the abdominal walls are thick or the muscles very rigid it is often most difficult to determine these points with certainty. A tolerably correct notion of the thickness of the liver may be formed during life in some cases in which a very flaccid state of the parietes allows the tips of the fingers of one hand to be placed upon its upper and those of the other hand against the under surface. In some cases of fatty liver this has been easily done, but the possibility of feeling more than an inch or two from the free margin is certainly exceptional.

Alterations in Consistence.—The consistence of the healthy liver is peculiar, and like that of other organs the liver becomes harder or softer at different times without necessarily departing from the healthy state. This is due partly to changes in the cells, but mainly to the varying quantity of blood in the vessels and of the interstitial fluid, which latter varies according as it is poured out or absorbed under varying blood pressure, and other circumstances.

Some idea of the consistence of the liver during life may be formed by feeling gently over the surface in cases in which the abdominal walls are not unusually thick or tense. In some cases we are able to get the fingers under the edge, and can clearly ascertain if the liver is unusually hard, as for instance in cirrhosis. The difference in the consistence of a fatty, a cirrhosed, and an amyloid liver may be detected during life in thin subjects, and it is sometimes possible to accurately determine by palpation the exact position of a hydatid cyst or of a hard or soft cancerous tumour, although the morbid growth may not perceptibly project from the surface. The fatty liver after death is generally harder and firmer than the healthy organ, but in extreme cases it becomes very soft. The amyloid liver is sometimes very hard and resisting. Deep pits or depressions may be made by strong pressure with the finger. The firmest and hardest texture ever acquired by the liver is produced by cirrhosis in cases in which the disease has slowly progressed during many years. In this disease almost all the soft hepatic tissue is slowly absorbed, leaving nothing but a very firm fibrous texture, which cuts like tendon, and is almost as dense and hard.

OF THE LIVER GENERALLY AND OF THE CONSTANT HEPATIC ELEMENT OR LIVER-CELL PRESENT IN ALL ANIMALS.

The liver is probably the most constant of all glandular organs, or perhaps it would be more accurate to say that an hepatic element exists even in the lower animals which are destitute of any apparatus or organ which deserves to be called a gland, at least in the sense that word is applied to the secreting organs of man and the higher animals. In the latter classes the liver is the largest secerning organ in the body. Its activity, commencing some time before birth, continues as long as life lasts. The liver suffers from many forms of temporary derangement as well as lasting disease, and anything which impedes its action or seriously interferes with the discharge of its functions, temporarily deranges the action of most of the organs and tissues of the body, and disturbs what is called the general health, while grave disease of the organ may cut short life in a few months or weeks, or even in the course of a very few days.

The great importance of the liver and of its healthy action was well known to the ancients, who, however, attributed to its powers actions and influences of the most extraordinary kinds, which, however, have been proved by modern investigation cannot with reason be attributed to it. But since we cannot even at this time give a clear account of the changes effected by this organ, we must not be too hard upon the conclusion arrived at when the means of investigation were very rough and imperfect. We have much to learn concerning hepatic chemistry if not of hepatic structural anatomy. Could the most profound of modern physiologists give conclusive and adequate answers to the following enquiries which might reasonably be made on the part of a student? Why do all or nearly all animals possess this special gland? Would the development of other organs proceed in the absence of the liver? In no case, I believe, has congenital absence of the liver been observed, though organisms have attained full development in which the liver has been less than half the usual size. Knowing as we do much concerning the nature and result of the work actually discharged by the lungs, kidneys, stomach, glands, and various parts of the brain and spinal cord, we are able to say in what respects the derangement of one of these organs would disturb the organism, while we are aware that if any one of them should be completely absent from some developmental defect or from serious disease development would not proceed; nay, in the case of damage or removal of some, life could not be sustained for any length of time. But the liver of the adult may degenerate or waste to

a degree that could not possibly occur in respect of any of the other organs, because death would have been caused long before the pathological change would have proceeded far in its course; and yet we know less concerning the action of the liver than of any one of the other organs mentioned. Looking only from the point of view of actual present physiological knowledge, we should perhaps feel inclined to conclude that the liver could be spared without creating more disturbance than is entailed by the loss of the spleen, supra-renal capsules, or some of the other organs—a conclusion which, however, has been proved to be erroneous by the fact that in health sudden serious injury to the liver is soon followed by death. Even violent concussion usually results in chronic and ultimately fatal structural change if at the time of the shock the liver was in a healthy state; while, on the other hand, if the organ had been already in a state of degeneration, it might bear a very violent shock without suffering any injury.

It must, I think, therefore be concluded that the liver is far more important to the economy than our actual present knowledge of its precise functions enable us to demonstrate or explain. Or, stating the point in another way:—The physiological action of the liver in health is yet so imperfectly understood that we cannot adequately account for its large size, its constant presence, or its unquestionable importance to the well-being of the organism.

In many of the lower forms of life the liver seems to be represented by what used to be called "cells" only, that is, by "elementary parts," which are composed of living matter, and are surrounded by formed matter consisting of substances resulting from changes in the first. This elementary part is really the essential thing, it is in fact *the liver element.* The living matter or bioplasm is endowed with the power of selecting certain constituents from the fluid which bathes the cells. It grows by appropriating these, and rearranges the elements of which they are made up, so that certain peculiar substances result which, by further chemical change, become resolved into the special matters endowed with very definite and remarkable properties, and which constitute the "secretion" of the liver-cell. Of the constituents formed by this cell some are again taken up and appropriated, and are destined to undergo still further complex chemical changes while others are completely removed, being driven through the intestinal canal as excrementitious matters, or after being taken up by the blood, are further oxidised, and at last transformed into products of excretion.

It is remarkable that in man and the higher animals the liver-cell should still exhibit its early characters, not only as regards the general nature of the secretion formed by it, but also in relation to the preparation of the food and its absorption and assimilation. The two classes of substances which it is the special office of the liver-cell

to elaborate seem to be formed in the lower as well as in the higher animals and man. Of these, one is taken up by the system and further changed, while the constituents of the other class are soon removed from the body like other products of excretion. From the beginning to the end of individual life we shall see the liver elementary part performing this two-fold office, and from the first appearance of a liver among the very low forms of existence to its ultimate and highest development in birds and mammalia, we find, besides biliary matters, glycogenic matter, as Bernard was the first to prove.

The liver is among the first of the glands to appear in intrauterine life, and it performs active work long before birth. That this is so is evident from the fact that gall-stones of considerable size composed of the very same substances that are produced in the liver of the adult have been found impacted in the duct of the infant at birth. These stones must have been formed long before birth, and must have gradually increased in size during the latter months of intrauterine life; for the materials constituting a gall-stone are very slowly deposited, and probably many weeks are required for as much cholesterine to be formed and deposited as would be sufficient to form a gall-stone large enough to obstruct the flow of bile along one of the larger ducts of the liver. I think it is probable that the formation and deposition of cholesterine commenced about or before the seventh month of intrauterine life.

The fundamental anatomy of the liver and the precise relation of some of its structural elements to one another have still to be determined. Many of those who have studied the subject are so divided in their conclusions on fundamental questions, that hopeless and incompatible doctrines have long been entertained and taught, and the particular view most favoured varies from time to time, and many a theory abandoned by one generation of anatomists has been revived and strongly advocated by a succeeding one. It is doubtful whether our views upon the structure and action of the liver as well as of some other organs and textures are now really in advance of some of those held by certain of our predecessors more than fifty years ago.

Possibly some anatomists would still be inclined to class the liver amongst the ductless glands, regarding the ductal part of the organ as the least important, although many authorities now-a-days seem to be leaning to the conclusion that the liver in its ductal arrangements is quite exceptional and unlike any other glandular organ, its secretion being carried away from the cells by ducts of extreme minuteness, passing either through their thin walls by permeation, or being conducted directly into very minute orifices which open upon the surface or are situated in the substance of the secreting cells. This view, as already remarked, necessitates the further conclusion that the liver of different sections of

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the animal series is arranged on fundamentally different principles,—an improbability which Hering has not only accepted but has even gone so far as to lay it down that the livers of fishes and reptiles are arranged according to a type-plan totally distinct from that which obtains in birds and mammalia.

Few observers appear to have realised the extraordinary difficulties involved in the acceptance of this view. For is it conceivable in the face of facts familiar to observers and demonstrable by anyone, that a gland almost universally present and apparently discharging some of the most essential and important functions of the organism, should be constructed upon principles so very different, that in orders so nearly allied as birds and reptilia the liver-cells should be situated outside the ducts in the one and inside their expanded extensions in the other? And is it not remarkable that the very confident statements of some anatomists appear to have led to the extraordinary generalization that the liver-cells are not directly concerned in the secretion of the bile, and this notwithstanding the fact known to all students, and to be demonstrated almost any day in certain morbid states of the liver, that biliary matter may be seen in the very substance of the cell itself? Again, as to the ductal part of the liver, which one would have thought sufficiently pronounced to have been entitled to careful consideration, it is scarcely credible that large works should have been written upon morbid changes in which the existence of small ducts seems to be almost ignored: while in the remarkable atlas published many years ago by Frerichs the ducts are altogether omitted in no less than twenty-six plates illustrative of various forms of hepatic disease. I shall, therefore, offer no apology for the numerous drawings I have made to illustrate the arrangement, distribution, and relations of the ducts and their extensions in the liver of man and many vertebrate animals; and it will not surprise the reader to find that the careful examination of and long familiarity with the ductal portion of the gland, have led me to adopt conclusions concerning the pathological changes in disease very different from those generally accepted at this time.

The mammalian liver is essentially composed of certain elementary structures, which are common to all secreting organs which possess ducts though differing much in structure and arrangement in different organs according to the precise work they have to discharge. This organ is, however, remarkable in this respect:—that part of the material elaborated by the special cells is not discharged with the special secretion of the gland, the bile, but is again returned to the blood.

The only constituent of the human liver which can be said to be common to all livers, and which is present through life from the earliest period of development to the most advanced age, and which

takes part in the essential and in most of the initial changes occurring in derangement, is the *Elementary part or Liver-Cell.*

To ensure the development and growth and the free and effective action of this important element, every other anatomical constituent of the liver seems to be subservient. Nor is it possible to conceive a disposition of parts more certain to effect the thorough removal of certain constituents from the blood which have accumulated therein, than that which actually exists in the arrangement of the capillaries and the hepatic cells in the human liver. Not only so, but the arrangement is such as to prevent the cells from undergoing deterioration in consequence of the great variations in the extent and rate of their action which takes place from time to time. Indeed, it is only in instances where from the reckless overwork to which they are subjected by those who eat and drink far more than is required, that any serious damage to the liver-cells is occasioned.

Each liver-cell consists of living matter (bioplasm) with a layer of matter formed by the first around it,—and which undergoes conversion into bile on the one hand, which passes into the ducts; and soluble and readily diffusible substances on the other, which, passing through the capillary wall, are returned to the blood, and are subjected to oxidation and other chemical changes in the circulation.

The *action* of the liver-cell probably includes the following changes: The living matter, particularly of the elementary part or cells near the surface of the lobule, takes from the fluid which transudes from the blood as this latter traverses the capillary vessels certain constituents which it appropriates. In this process the elements of the substances become rearranged, and so placed with respect to one another that new compounds shall be at length formed. To reach the bioplasm or living matter, the liquid pabulum having the proper compounds dissolved must traverse the formed matter of the cell which undergoes gradual increase in amount as the cell increases. The flowing towards the bioplasm of currents of fluid is due, I think, to the tendency of the particles of the living matter to move away, such tendency necessarily causing a flow in the opposite direction. By the death and conversion of a certain amount of bioplasm new formed matter is produced on its surface, while at the outer part of the elementary part a certain amount of the oldest part of the formed material is gradually broken down, and resolved into the numerous products, many of which are of highly complex chemical composition, constituting the secretion of the cell.

By coagulation and other changes occurring after death, and by the use of some reagents, certain lines indicating networks or a reticulated stroma become apparent in the substance of the cell. Such appear-

ances have been believed by many observers to indicate a peculiar structural arrangement which they think has much to do with the special work discharged by the elementary part. This disposition to explain action by structural arrangement has increased of late years, and not a few incline to the general conclusion that the formation of various products and the performance of special actions will ere long be found to depend upon structural peculiarities, just as the formation of particular structures is referred to peculiarity of chemical composition. Not only are both these assumptions devoid of any foundation in fact, but they are rendered untenable by what is known concerning the processes in question. Not a few of the very delicate irregular lines seen in some liver-cells, and in the cells of other tissues and organs, for the most part converge towards the nucleus (the bioplasm) of the elementary part, and very probably represent the paths taken by the fluids holding various substances in solution as they pass towards the living matter. In each elementary part during life, currents to and from the living matter are constant, and as we see in the hair-like bodies of the flower of Tradescantia, the course of these currents is not straight, but in irregular lines, which alter from time to time in position and direction. The fluid which ebbs and flows differs in composition from the intervening substance, which, however, during life is no doubt itself semi-fluid. Many of our reagents precipitate some of the constituents of the fluids occupying the channels, and in this way the lines become fixed and clearly marked.

The secretion having been formed passes away from the cell into ducts, and continues to undergo further changes as it traverses the efferent channels, some substances permeating the walls of the ducts and passing again to the blood, while the solution of other constituents becomes gradually concentrated. The efferent ducts commence as wide excessively thin-walled tubes, which, as I shall endeavour to prove, contain the hepatic cells. The secretion therefore passes directly from the cells into the ductal part of the gland.

The system of efferent hepatic ducts is very extensive, and their arrangement is remarkable. Their course through the liver, the structure and arrangements of their coats, the provision to ensure the passage of the secretion through a duct—even should a large branch be obstructed—are all worthy of the most careful attention of the physician, as well as of anatomists and physiologists. Indeed, every one who studies the general structure of the vertebrate liver will be forcibly struck with the wonderful arrangement of its constituent anatomical elements. He will not fail to notice how the same disposition of the parts which effects economy of material, also serves to provide for and ensure the most thorough and complete action of the cells upon the blood, as it passes through the capillaries of the lobule, for these are

completely surrounded by the secreting cells, being only separated from the latter by the excessively thin capillary wall.

The vessels by which the blood is brought into close proximity with the cells or elementary parts of the liver are arranged unlike those of any other organ. For the capillary network is many times more extensive than that in any other organ, and while the bulk of the blood which traverses it consists of venous blood, which has already passed through the capillaries of different parts of the intestinal canal, a small quantity of arterial blood is mixed with it, and probably acts by oxidising some of the compounds dissolved.

The capillaries of every part of the lobule converge towards the centre, where a small venule, capable of much alteration in capacity by reason of contraction and relaxation of the muscular fibres of its coat, receives the blood. Pl. II, Fig. 7. Soon uniting with others from adjacent lobules, veins of considerable size are formed. These may be seen in considerable numbers cut across in a section of the liver made in any direction. Pl. II, Figs. 3, 7, page 40. It is remarkable that observers should not have realised the vast extent of the lobular capillary network. No drawing I have yet seen, even in the most recent works, seems to me to convey an adequate idea of the arrangement as it exists in nature. My Fig. 7 is as accurate a copy of the preparation as I could make, but I doubt whether it contains as many capillaries between the branches of the *interlobular* or portal veins, and the *intralobular* or hepatic vein as exist in some of the larger lobules of the human liver.

The unusual extent of the capillary network of the lobule of the liver, and the exceeding tenuity of the capillary walls, lead us to infer that the change required to be produced upon the blood as it passes through the vessels is of a very important character, and that it has to be thoroughly and completely effected. The actual arrangement which exists as regards the capillary network of the liver of birds and mammalia is such that it is, indeed, hardly conceivable that even the smallest quantity of blood laden with new materials, recently absorbed from the intestine, could reach the vein in the centre of the lobule, without having been subjected to the full influence of a great number of hepatic cells.

MINUTE ANATOMY OF THE HUMAN LIVER.

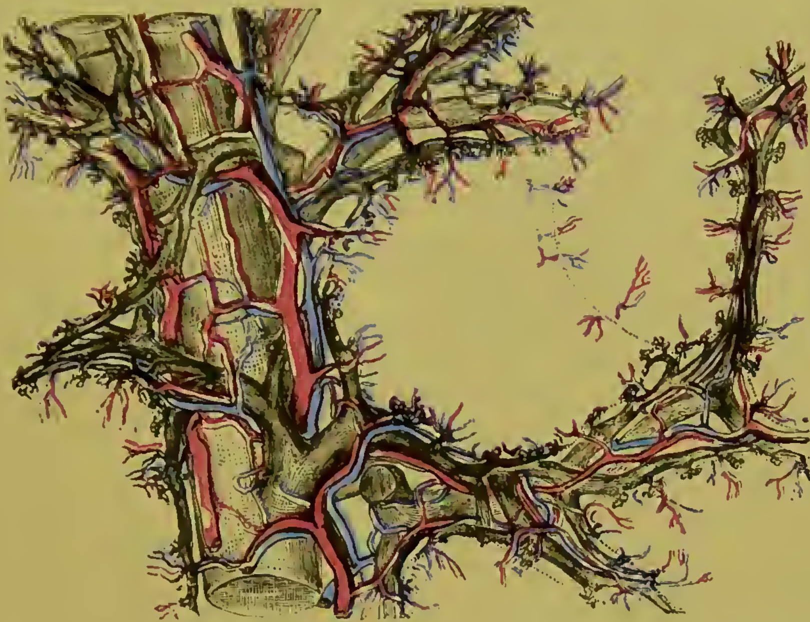
In the compact mammalian liver there are two important series of channels, which in their ultimate distribution may be said to alternate with each other. The one contains a branch of the portal vein, hepatic artery, and hepatic duct, with lymphatic vessels, large and small, and nerve-trunks. The other series contains a branch of the hepatic vein alone, and the small vascular branches by which the coats of the veins are supplied with blood. This arrangement ensures that there shall be an equable as well as free distribution of the blood to the capillaries of each individual hepatic lobule, and a very free carrying away of the blood from the lobule as soon as the proper changes have been effected in it by the action of the cells to which it has been so thoroughly exposed. By the arrangement of the blood-vessels and the passage through them of the blood as it traverses the capillaries, the carrying off of the bile after its elaboration is facilitated.

PORTAL CANALS.

From the transverse fissure of the liver the first set of tubular passages, known as the *portal canals*, may be traced and followed as they ramify through the liver in every part of its substance, those most distant from the larger branches being the smallest. Each portal canal contains branches of the vessels above enumerated, and by this arrangement it is provided that no part of the hepatic tissue shall be at a greater distance from one of the portal canals than about one-sixtieth of an inch. The distance is nearly equal in every part of the liver of the same species, but different in different classes and species. The tubular passages above referred to were called Portal Canals by Mr. Kiernan, and are represented in Pl. IX, Fig. 27, p. 64, which has been copied from Mr. Kiernan's figures in his paper in the "Phil. Trans." The general course which the portal canals take in the livers of different animals varies much, some being highly tortuous and irregular in their distribution, while in other cases, as in the rabbit, the canals seem to radiate in a surprisingly regular manner from the transverse fissure towards the circumference of the liver. In the seal the direction of the portal canals is much nearer that of a straight line than is the case in the human liver. When the liver is very thick, the course of the portal canals is tortuous and less regular, and one canal is seen to occupy many different planes in a very limited part of its course.

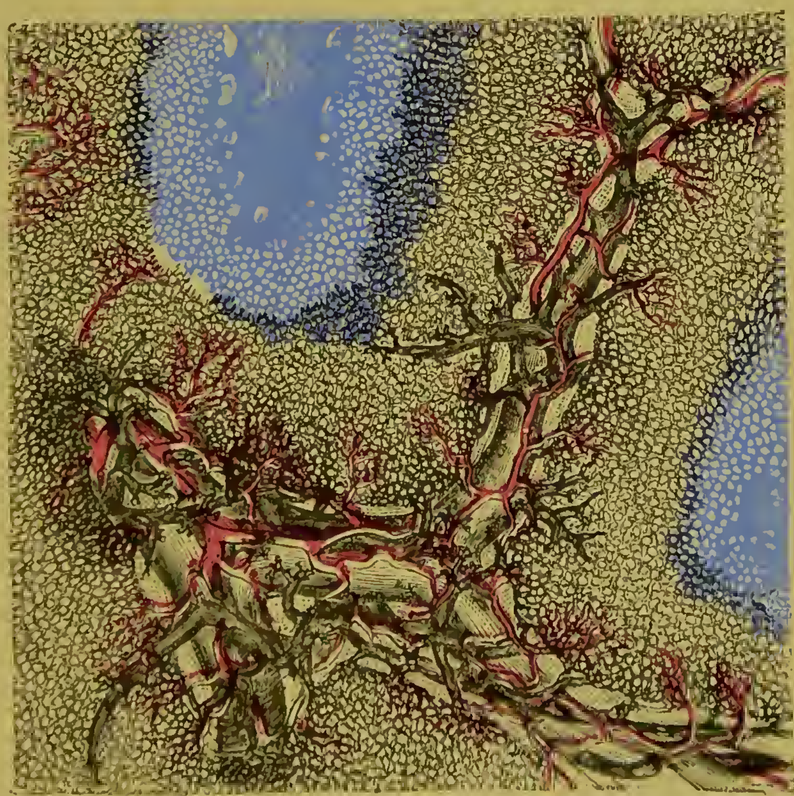
VESSELS AND DUCTS.—HUMAN LIVER.

Fig. 1.



Branches of portal vein, hepatic artery and hepatic duct as seen in a portal canal or interlobular fissure. From the human liver in which the portal vein was injected with white lead, the artery with vermilion, and the duct with Prussian blue. In the figure the portal vein is not coloured. The hepatic artery is red and the duct blue. × 40. pp. 41, 42, 46.

Fig. 2.



Portions of three lobules of the human liver in which the portal vein had been injected with carmine, the hepatic vein with Prussian blue, and the artery with vermilion. In the figure the portal vein is not coloured. The artery is red and the hepatic vein with capillaries near it, blue. Duct not shown. × 60. p. 40.

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In sections of the human liver the smallest canals alternate in the manner described, and seem as it were to interdigitate with the hepatic venous canals, the proper hepatic tissue occupying the intervening space. In sections of the liver in which the smaller branches of the vessels have been cut across at right angles, the cut areas of a small hepatic vein will occupy the centre of a portion of hepatic tissue, a certain distance from which will be seen divided branches of the portal vein, hepatic artery, and duct arranged at short intervals, marking the circumference of a lobule, and forming a boundary line between adjacent lobules. The arrangement is represented in Pl. I, Figs. 1 and 2, where branches of the portal vein (circumferential) are well seen in spaces between the lobules, and those of the hepatic vein in the centre. In these figures the vessels are all much larger than in the natural state, in consequence of being over-distended by the injection, but they are accurate copies of the preparations. When a section is made across the liver, and the lobules are cut through, each small branch of hepatic vein (intralobular) is seen to occupy the centre of a piece of hepatic tissue (lobule), which is bounded on its circumference by small branches of portal vein, hepatic artery, and hepatic duct (interlobular), which ramify on the outer part of the lobules, and give off branches which at once pass into the substance of the lobule, as shown in Figs. 1 and 2, Pl. I. Branches of vessels which ramify in the portal canals on reaching the lobules lie in spaces between them, which have been called the *interlobular fissures*. The triangular interval left by the approximation of three lobules, which is, in fact, a section of a small portal canal or interlobular fissure, has been termed the *interlobular space*.

PORTAL VEIN.

The smaller subdivisions of the portal vein reach the circumferential part of each lobule at several points of the surface or circumference, and one small branch often gives off twigs to the neighbouring lobules, so that the vein divides in a stellate manner. The branches upon different sides do not anastomose so as to encircle each lobule with a venous ring, as many authors, following Kiernan's figure, which does not pretend to be more than diagrammatic, have even recently described and represented, but branches of the vein communicate with one another only through the intervention of capillaries, as Bowman, Kölliker, and some other observers have stated. Gerlach gives drawings of the assumed anastomosing trunks, the diameter of which he represents as the same round the entire circumference of the lobule, an arrangement which certainly does not exist in nature, and which cannot be made by any process yet discovered. Even in the pig there is no vascular ring, although, in some injections, to the unaided eye it

appears as if there were. In the liver of the human subject, and in livers allied to it, small separate branches of the portal vein can often be isolated and followed from the interlobular fissures into the lobule, breaking up into smaller vessels as they approach their final subdivisions into capillaries. The arrangement is represented in Figs. 3, 7, and in Fig. 33, Pl. X, from the human liver. The manner in which the smaller branches of the vein divide and subdivide on the surface of the lobule is well shown in the figures in Plate I, which have been carefully copied from specimens prepared by myself. The branches of the portal vein were injected with white lead, and their mode of division and subdivision is well seen. Branches of the duct and of the artery filled with differently coloured injections could be well traced, and have been carefully copied in the figures.

In Fig. 2 the capillaries are seen, and these have been accurately copied, as regards both arrangement and dimensions. Those in the central part of the lobule have been filled from the hepatic vein with an injection of a different colour. This capillary system of the hepatic lobule is more extensive than any other in the body, and the blood in passing from a branch of the portal vein traverses a far greater extent of capillaries before it is poured into the branch of the hepatic vein in the centre of the lobule than in any other organ of the body, not excepting even the lung.

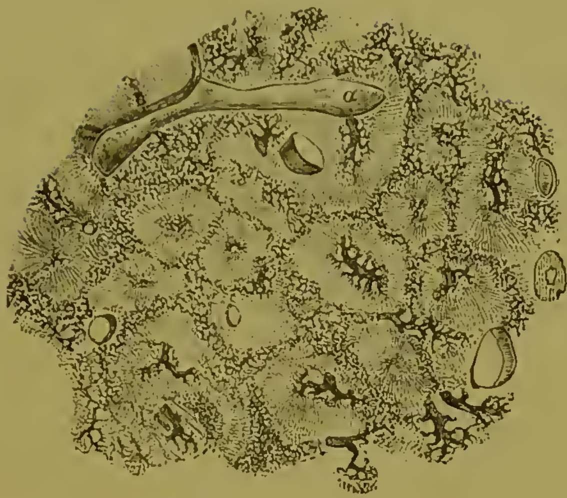
Manner in which the Appearance of a Venous Ring round each Lobule is Produced.—By their mode of ramification, as has been shown, the smaller portal vessels more or less imperfectly enclose little portions of liver which vary somewhat in form in different animals, and according to the manner in which the section is made. These have been called *Lobules*. Plates I and II, Figs. 1 to 7.

In the majority of animals the secreting structure and capillaries forming the substance of one lobule, communicate with those of the adjacent ones in the intervals between the channels by which the branches of the vessels reach the lobules. Fig. 7, Pl. II, at *a*, Fig. 2, Pl. I, *a*. In the pig, however, each lobule seems to be invested with a thin capsule, and seems to be distinct except that the little branches from the vessels pass in opposite directions from the small trunk to the adjacent lobules, which cannot, therefore, be separated from one another without tearing the vessels.

In dried preparations, owing to the close approximation of trunks which in the recent state had occupied very different planes, an appearance as if the smaller trunks communicated with each other, and thus encircled the lobule in a venous ring, is undoubtedly produced when the specimen is examined by low magnifying powers. That such an appearance is fallacious is proved by carefully examining well injected specimens in fluid. For this purpose it is better to use a transparent

LOBULES OF THE LIVER.

Fig. 3.



Thin section of human liver showing arrangement of lobules. *a* Section of a large branch of portal vein. The branches of the portal vein are well seen (interlobular). The hepatic veins (intralobular) are seen in the centre of the lobule. × 8.

Fig. 4.

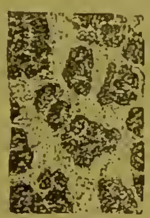
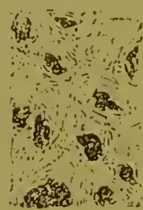


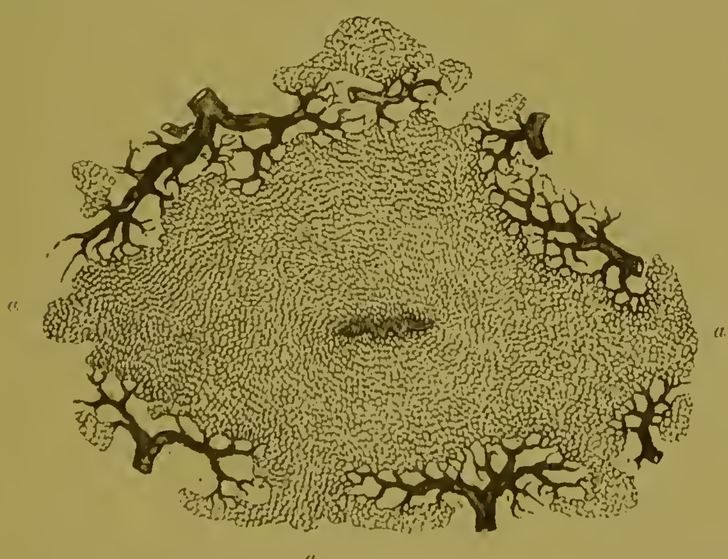
Fig. 5.

Fig. 6.



Human liver in cirrhosis. Showing three stages of the disease. The gradual wasting of the secreting hepatic tissue proceeding from the circumferential part of each lobule towards the centre, and its degeneration into a form of connective tissue, of which the hepatic tissue seems in extreme cases to almost entirely consist. Each lobule seems to get smaller as the disease advances, but the appearance really depends upon the degeneration of the lobule in its circumferential part. × 3. p. 42.

Fig. 7.



A thin section of a lobule of a healthy liver, the portal and hepatic veins having been injected with different colours. The extensive capillary network connecting the terminal ramifications of the portal vein with the central branch of the hepatic vein are shown. At *a* the capillaries of one lobule actually communicate with, and are continuous with, those of adjacent lobules. Portal vein and capillaries (interlobular) not coloured. Hepatic vein and capillaries (intralobular) darker. × 40.

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injection, which can be examined by transmitted light. Very rarely, however, small branches of the vein do anastomose, but such direct communication is quite exceptional, and a similar anastomosis even occurs, sometimes between branches of the hepatic vein. The representations of many authors are very diagrammatic, and would lead to the conclusion that a ring formed by branches of the portal vein, round the circumference of the lobule was constant, while no such arrangement has ever been seen.

By this gradual subdivision of the small trunks of the portal vein, as it approaches the margin of the lobule (Plates I, II), it is obvious that the area of the resulting branches must be enormously augmented, and in consequence a gradually increasing slowing of the rate of the flow of blood as the capillaries are approached must result, a state of things very favourable for the removal of various constituents of the portal blood by the action of the cells.

Pathological and Clinical.—Very little observation in the post-mortem theatre will suffice to convince the observer of the very varying capacity of the branches of the portal vein in different livers. This difference is not due merely to differences in size of the organ itself, but results from a number of circumstances connected with the activity of the liver-cells, and the rate of their growth, which differs much in different individuals. The quantity and nature of the food and liquid taken, as well as quantity of the blood, the amount of muscular work, and less directly the activity of the respiratory process, will exert an indirect influence in determining the size of the branches of the portal vein in the liver. If the liver-cells act slowly and imperfectly, while a very considerable quantity of food be taken, and especially if the lacteals are not very active, the large quantity of blood circulating through the intestinal vessels, and poured into the portal vein, will accumulate in that vessel and its larger branches in the liver, instead of traversing the capillaries of the lobule as fast as the blood reaches them. The large and small subdivisions of the vein will dilate, and thus is sometimes formed what is practically an extensive reservoir in which a very considerable quantity of blood may collect. In some cases the small veins in the portal canals, those distributed to the gall bladder, those in the transverse fissure and in the capsule of the liver, as well as the ordinary branches of the vein, become considerably dilated. The pressure thus induced is as is well known to some extent relieved by much of the blood regaining the inferior cava without passing through the liver at all, through such venous communications as are established with the renal, hæmorrhoidal, and inferior mesenteric veins. But, nevertheless, dilatation of the veins proceeds, and much blood not properly depurated by hepatic action gets into the general circulation, and exerts a deleterious effect.

Frequently recurring distension of the portal vein after some time results in permanent dilatation of the branches of the vessel. The coats first become stretched, and then in many cases infiltrated with lymph, which gradually undergoes conversion into fibroid tissue, which slowly contracts, and thus thickening and condensation of the coats, with more or less adhesion of the external coat to the tissues around is occasioned, so that when the vessels are cut across the tube remains open, and shows a much larger area of section than normal. The changes in the portal vein above referred to give rise to alterations in the hepatic structure, which may at length result in diminution and wasting of the liver-cells. This is one way in which contraction of the liver is brought about. Pl. II, Figs. 4, 5, 6.

The engorgement of the veins above referred to is among the many causes of enlargement of the liver. The increase in size will extend over a short or long period of time, according as it is due to mere accumulation of blood in the vessels, or to this and some degree of infiltration into the hepatic tissue. The medical management of such cases almost resolves itself into the maintenance for a time of moderate purgation. In this way the removal of the watery part of the blood is effected, and the tension of the vascular walls is much relieved. A carefully regulated moderate diet, with a very limited supply of fatty and albuminous materials, but consisting mainly of farinaceous matters, easily digestible vegetables and fruit, should be given, and the patient made to rest in the recumbent position.

HEPATIC ARTERY.

In each of the larger portal canals there are several branches of the hepatic artery, Pl. I, Figs. 1 and 2, and division and subdivision of the smaller ramifications of the vessels may be followed over the portal vein and hepatic duct, to the coats of which latter vessels especially a large proportion of arterial blood is distributed. In the larger portal canals and in the transverse fissure many small arterial branches are irregularly distributed amongst the areolar tissue.

Branches to the Capsule.—Many branches of the artery pass to the capsule of the liver, in which they ramify abundantly, forming a network having large meshes. These capsular branches and their anastomoses are readily injected in the liver of the fœtus or child. They are beautifully seen upon the surface of the pig's liver, and encircle each individual lobule with an arterial ring.

Branches in the Portal Canals.—Each branch of the portal vein, in the small portal canals and interlobular fissures, is accompanied by at least one branch of the hepatic artery, and generally by two or three

which communicate with each other by anastomising branches. Pl. I, Figs. 1 and 2.

Each artery gives off numerous branches in the portal canals. The greater number of these are distributed upon the coats of the ducts. The thick walls of the larger ducts are thus abundantly suppled with arterial blood; but the smaller branches of the duct, the coats of which are extremely delicate, pass through the meshes of an arterial network, as represented in Fig. 10, Pl. III, p. 48. In the pig this network may be very readily demonstrated upon the surface of each lobule; but in the human subject, and in mammalia generally, the branches are less numerous, and are seen only in the interlobular spaces. Small arterial branches, also, supply the coats of the portal and hepatic veins. The greater quantity of blood, after passing through these arterioles, is collected by venous radicles, which empty themselves into branches of the portal vein, prior to their subdivision into small interlobular branches.

Branches which open into the Portal Capillaries of the Lobule.—A certain proportion, however, of the blood is undoubtedly poured into the capillaries of the lobule, as may be readily proved by injection with different colours. Some very small straight arterioles may be traced from the portal aspect of the lobule, or from the interlobular fissures, for a short distance into the interior, where they join the capillaries, near the portal surface of the lobule. Pl. I, Fig. 2.

The whole of the arterial blood, therefore, which carries oxygen to the several parts of the liver, passes through the capillaries of the lobules before it is returned to the heart, and no doubt furnishes a small portion of the material from which the bile is formed. The hepatic artery was originally regarded by Kiernan as one of the sources of the blood conveyed to the secreting structure of the liver, by the branches of the portal vein. (*Op. cit.*, p. 748.)

Diameter of the smallest Arterial Branches.—The *meshes* of the network which the smallest branches of the artery contribute to form, are many times wider than those of the venous capillaries in the lobule; but the diameter of the small vessels of which this network is composed is very much less than that of the portal capillaries. I have measured the diameter of the smallest arterial branches in the pig and in the human subject. The average measurements were as follow; but these numbers must be considered rather as approximations to the truth than as absolutely correct, because it is impossible to ascertain to what degree the vessels have been distended by the injection:—

	Pig.	Human.
Smallest branches of artery ...	1-4000th of an in.	1-4000th of an in.
Venous capillaries of lobule ...	1-1600th ,,	1-1300th ,,
Small ducts on surface of lobule ..	1-1600th ,,	1-1800th ,,
Finest portions of duct	1-2500th ,,	1-1800th ,,

Injection of the Venous Capillaries of the Lobule from the Artery.—That the capillaries of the lobule can be injected from the artery necessarily follows from the nature of the arrangement just described. In this way, Lieberkühn injected the lobules from the portal as well as from the hepatic veins. As a general rule, the injection appears first quite at the portal surface of the lobule, and gradually extends towards the centre; but sometimes the central capillaries are injected from the artery very readily, while the marginal capillaries are quite free from injection. This has occurred to me in the human subject and also in the pig; but it was confined to certain small portions of the liver, while in the greater part of the organ, small arteries could be readily traced into the marginal capillaries. In the situations referred to, the branches of the portal vein were very imperfectly injected, and the capillaries did not contain any injection, in consequence, probably, of being filled with fluid previous to injection, while the central capillaries were empty. The explanation of this circumstance I imagine to be this—that the injection having found its way by one channel into these central capillary vessels, gradually spread through them, until the appearance above referred to was produced, the course of the injection towards the portal capillaries being, in the majority of instances, prevented by their distension with blood or serum. If the preparation exhibiting this arrangement be compared with others from the same liver, its mode of production can be clearly made out. I think the fact explains the result obtained by some anatomists, who have been led to conclude, from the appearance above indicated, that the small arteries emptied themselves into the capillaries nearer to the intralobular vein, or into this vessel itself.

The whole of the blood, therefore, which has become venous after passing through the arterial network, mixes with that of the portal vein, either before the trunk divides in the liver, or into the large branches in the portal canals, or into the lobular capillaries.

The Uses of the Arterial Blood.—It has been often asserted as a general proposition that the arterial blood distributed to tissues and organs is required for the nutrition of the anatomical elements rather than for their action; indeed in not a few instances is the artery called a "nutritious artery," in accordance with its supposed function. Many facts to which I have drawn attention conclusively indicate that arterial blood is not requisite for nutrition. Many of the most rapidly growing textures are solely dependent upon venous blood. A careful review of the facts will, I think, thoroughly convince anyone that the oxygenised blood takes part in the oxidation of substances which at length pass away as products of secretion of the gland. The remarkable distribution of the artery, and the large size of the frequently anastomosing branches distributed to the gall bladder and to the ducts of

the liver, can scarcely be explained upon any other supposition. The arterial blood poured into the capillaries of the lobule near its circumference, no doubt supplies oxygen which takes part in the oxidation of some compounds, which at length become constituents of the bile. If the arteries degenerate, or the arterial blood from any cause be imperfectly oxygenated, the chemical changes dependent upon the oxygen are but imperfectly performed, the secretion becomes altered, and incapable or less capable of performing its office; digestion is impaired, and the body soon suffers in its general nutrition. It is probable that if the supply of oxygen be imperfect, substances which ought to be converted into carbonic acid, or some highly oxidised product, attain only an inferior degree of oxidation, and assume a form in which they cannot be carried off, to the detriment of the action of the liver, and perhaps occasioning morbid change.

Of the Vessels of the Gall Bladder, Transverse Fissure, and Portal Canals of the Human Liver.—The very peculiar arrangement of the vessels of the gall bladder is referred to in my memoir on "The Anatomy of the Liver," "Phil. Trans.," 1855. The only author who previously noticed this beautiful disposition of the vessels is Professor E. H. Weber,* but he makes no mention of a similar arrangement of the vessels in the transverse fissure and in the portal canals; and it is surprising that, as least as far as I can ascertain, no observer has yet figured the very remarkable disposition of these vessels, shown in Pl. III, Figs. 8, 9, p. 48. The gall bladder, the transverse fissure, and the portal canals are, as is well known, abundantly supplied with arterial blood, especially in the neighbourhood of the ducts. In these localities there exists a remarkable arrangement for the free circulation of the blood through the arteries, and its return into branches of the portal vein. Each branch of artery is accompanied by two branches of the vein, and this arrangement exists even in the case of very small divisions. The small branches of the arteries anastomose very freely, in some cases forming five or six-sided spaces, so that an arterial network is formed. Pl. III, Figs. 8, 9, and 10. This is wonderfully developed on the external surface of the gall bladder. Each artery composing this network is accompanied on either side by a branch of vein. These also form networks, and the two venous branches communicate freely with each other, by transverse branches which pass over or under the artery. The trunks of the veins and arteries are of course distinct, and the blood, as in other cases, passes through capillaries before it reaches the veins, but the capillaries are themselves wider than the average, and

* "Annotationes Anatomicæ et Physiologicæ. Programmata Collecta Fasciculus II," p. 225. "Berichte über die Verhandlungen der Königlich Sachsischen Gesellschaft zu Leipzig," No. III, 1850, s. 185.

the anastomoses between the smaller branches of the vessels before they pass into the capillaries are very numerous.

The larger branches of the vessels described are from the 8th to the 20th of an inch in diameter. Such an arrangement of double veins facilitates the rapid return of the blood after it has passed through the arteries, and, as each branch of the vein is as large as the artery, a larger quantity of blood than is transmitted by the arteries in a given time might return through the veins, in case the volume of blood should be suddenly increased by the rapid absorption of fluid.

The hypothesis that the arterial blood distributed to a gland is required for the nutrition of the structures of which the gland is composed, will not explain the large or small amount of arterial blood sent to different parts of an organ, nor does it account for the distribution of so large an amount of arterial blood in the wall of the gall ducts, or in the coats of an organ like the gall bladder. Many facts seem to establish the conclusion that the arterial blood exerts a very important influence in the process of secretion generally, and, in some instances, upon the secretion itself after it has been formed. It is certain that the bile is subjected to the action of the oxygen of the arterial blood in every part of its course, from the smallest ducts with walls composed of the thinnest possible membrane, till its arrival at the common duct or gall bladder. While it remains in this viscus further changes are exerted in it by the arterial blood so abundantly distributed to the mucous membrane by very numerous vessels, which consist of small trunks in great number as well as capillary vessels. Besides this, in the peculiar arrangement of the veins, we cannot fail to see a special provision to promote the free return and very rapid renewal of this blood, although its bulk has been increased by the absorption of water from the bile as it traverses the ducts, and undergoes inspissation. One large vein would be much more likely to have the circulation through it impeded by pressure or stretching, than two smaller ones, and as the calibre of each of these veins is nearly the same as that of the artery between them, any circumstances tending to retard the return of blood in the veins would also diminish the flow in the arteries, so that this arrangement provides, in the most perfect manner, for the free circulation of the blood under all circumstances.

Through the kindness of the late Professor Weber, I had, in the year 1857, an opportunity of reading his researches upon the anatomy of the liver, in which he refers to the distribution of the vessels upon the gall bladder. Weber is the only author who seems to have drawn attention to this very beautiful and unusual arrangement of the vessels. The large proportion of arterial blood traversing the arteries, and its free and rapid passage into the large veins, indicate that some change is effected in the bile beyond the mere absorption of water. The arrange-

ment described is evidently connected with oxidation. The wonderful arrangement of the *venæ comites* is not easy to account for, but it is very remarkable, and it is found to the extent here demonstrated as far as I am aware in this organ only. The free distribution of large arterial branches to the coats of the gall bladder and to the ducts in the portal canals, the close proximity of anastomosing small arterial branches to the diverticula of the ducts, the fact of the communication between the arterial ramifications and the portal capillaries near the circumference of the lobule, where disintegration and bile formation are proceeding rather than near the centre of the lobule, where growth and nutrition of the cells are more active, clearly indicate, as it seems to me, that the arterial blood is concerned in distributing oxygen to the liver rather than that it is employed for furnishing substances required for the nutrition or growth of the secreting or other anatomical elements of the liver.

HEPATIC DUCT.

Considering the large size of the liver, its constant presence in all animals, the large quantity of its secretion which is carried away, and performs important ulterior offices, and, at least in vertebrata, the conspicuous character, long course, and considerable capacity of the ducts, it is remarkable that more persistent attention has not been given to the origin and general arrangement of the channels by which the bile is received and carried away from the thousands of lobules where it is secreted.

As regards the arrangement of the smaller ducts, which can without difficulty be demonstrated in ordinary injections, there is still much difference of opinion, while some authorities appear to attach such little importance to these channels in the development and progress of morbid changes of the proper secreting structure of the liver, that some almost ignore the ducts, and describe and figure with elaboration and minuteness the results of grave pathological changes without delineating a single duct, although in the alterations which have taken place these tubes have really played a highly essential part, and have, in many instances, undergone changes as extensive and as decided as any which have affected other tissues of the liver.

Although it may be true that certain offices of the liver other than bile formation are of very high importance, there is no doubt that the delivery of the bile into the upper part of the small intestine is a very essential part of the hepatic office, and it will greatly mar the completeness of the general view we take concerning the cause of the existence of the liver, and the functions it discharges in the economy if we at all underrate the importance of bile formation, its discharge into the intestine, and subsequent change.

A large branch of the duct lies in each portal canal, with a vein and one or more branches of the artery. At least one branch of the duct accompanies each branch of the portal vein, but frequently there are two or three. From the branch or branches of duct accompanying the vein, several smaller ones pass off to the secreting structure of the lobules near. These do not anastomose so as to encircle the lobules. In the pig, the interlobular ducts, while running between contiguous lobules, are applied, as it were, to the exterior of the capsule of each, and give off much smaller twigs on either side (Figs. 34, 35, Pl. X, p. 64), which perforate the capsule, and become connected with the secreting structure.

The coats of the larger ducts are thick and firm, and are capable of resisting strong pressure without giving way. The fibrous-like tissue of which the walls are mainly composed, must be almost impermeable, and no one carefully looking at their texture would, for a moment, entertain the idea that through such tissue the watery part of the bile would readily pass, and be taken up by the vessels, particularly veins and lymphatics, which ramify in considerable number outside the duct.

It is remarkable that in the thick walls of many of the large ducts are found in most animals numerous little cavities opening upon all sides of the interior of the tube. In the human liver in which, according to my own observations, their form is very irregular (Pl. V, Figs. 11, 12, 13, 14, Pl. VI, Fig. 18), they open by a line of orifices on opposite sides of the duct, as Kiernan described. These cavities have been generally looked upon as mucous follicles, but they are better termed *Parietal Sacculi*, because their form is not always such that the term *follicle* can be correctly applied to them. Neither has it been satisfactorily shown that they are concerned in the secretion of the mucus of the bile. At the point where a small duct opens into a larger one, the lining membrane is often so disposed as to form a valve which would tend to prevent the passage of the bile from the large duct back again into the smaller branch, while it would not in any way interfere with the free passage of the fluid in the opposite direction. The small branches coming off from larger ones make an acute angle with the trunk, and often run obliquely for some distance in the substance of the coats of the larger duct.

Parietal Sacculi.—In the coats of ducts about the 1-125th of an inch in diameter, and in larger ones, many little saccular dilatations are situated. In the pig, and in many animals which I have examined, they are arranged all round the tube. Figs. 16, 17, Pl. VI. They may be described, for the most part, as simple oval pouches, connected with the cavity of the duct by a very narrow neck, which in the pig is often less than the 1-10000th of an inch in diameter. Pl. VI, Fig. 17. In the

VEINS AND ARTERIES.

Fig. 8.

Vessels of the human-gall bladder, as seen from the outer surface. The artery was injected with vermilion, and is the central vessel left white in the cut. The vein was injected with white lead, and is dark in the drawing. One branch of vein is seen on each side of every branch of the artery. One half larger than natural. p. 45.

Fig. 10.

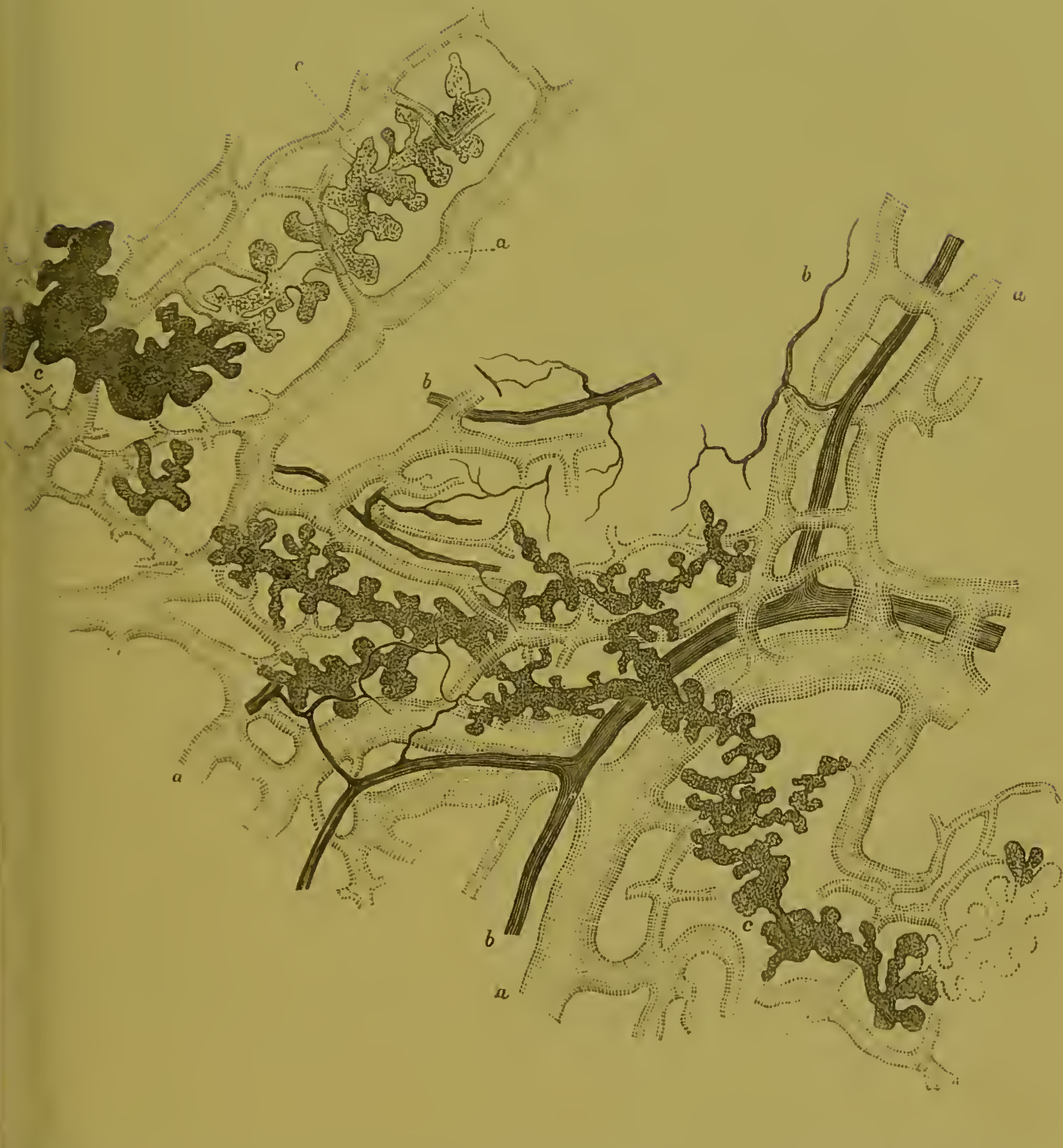
Vessels in a portal canal of the human liver injected. The *central dark* vessel is the artery. The veins have been left light. Two accompany each branch of artery as in the gall-bladder. Natural size p. 43.

Fig. 9.

A portion of Fig. 8 more highly magnified. × 20. p. 45. The regularity of the arrangement of the small veins is very remarkable.

VASA ABERRANTIA AND VESSELS.

Fig. 10



aberrantia connected with the ducts. Branches of the portal vein and hepatic artery from the transverse fissure e human liver. The vasa aberrantia injected with Prussian blue. Some of the branches and sacculi are only rfectly injected, and some are not injected at all. The vein *a* with white lead. The artery *b* with vermilion. × 42. p. 49.

B., AD. NAT. DEL., 1854.

[To follow Plate III.

PLATE V.

Fig. 11.

Fig. 12.

…erlobular duct with lateral appendages and inter-communicating vasa aberrantia Human. × 8. p. 49.

Fig. 13.

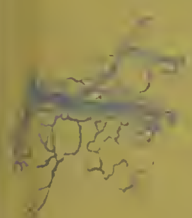
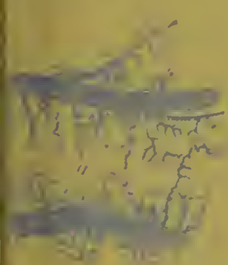


Fig. 14.



…s. 13 and 14. Ducts with …merous vasa aberrantia …d anastomosing ducts …h form networks in…ed with Prussian blue. …ral size. Transverse fissure. Human liver.

Fig. 15.

A part of the convoluted portion of a uriniferous tube from the newt's kidney, showing capillary vessels and nerve fibres. The thickened 'basement membrane' of the tube is continuous in structure with the connective tissue of the kidney. The nerves ramify upon and in this membrane, but do not pass into the interior of the tube and reach the secreting cells. × 315. p. 51.

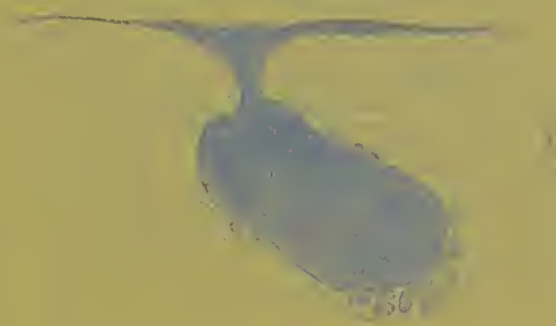
…S.B., AD. NAT. DEL.

[To follow Plate IV.

Fig. 16.

…lar duct with parietal sacculi of the pig, …h are situated in the coats o the duct, …surface of which is represented in outline. *a* Branch of artery. p. 48.

Fig. 17.



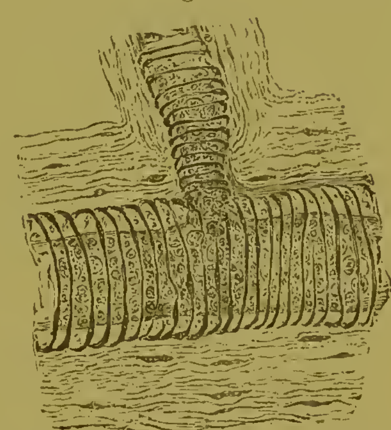
a Fig. 16 × 215.

One of the sacculi × 215 well filled with injection. At the lower part of the drawing is seen the epithelium forced to the lower part of the cavity by the injection. p. 48.

Fig. 18.

…ular duct with lateral appendages and some irregularly branching parietal …and vasa aberrantia. The greater number of the lateral channels do not beyond the outer surface of the fibrous coat of the duct. × 15. p. 48

Fig. 19.



Portion of a duct of lophius piscatorius showing the epithelium of the duct within, then a layer of circular muscular fibres, and externally longitudinal fibres constituting the outer part of the duct. × 215

[To follow Plate V.

larger ducts, the sacculi of the ducts are branched, and often run for some distance in the coats. Occasionally the branches of one sacculus anastomose with those of another. The largest in some animals, as for example in the squirrel and sheep, are singularly complicated, and project some distance from the duct, lying in the areolar tissue which surrounds it.

In the human subject a somewhat different arrangement occurs. Instead of being situated entirely round the tube, the openings form two rows or lines, situated upon opposite sides of the ducts, as already described. The greater number of these openings are, however, the orifices, not of sacculi, like those in the pig, but of small irregular tubes, which run obliquely for some distance in the coats of the duct and anastomose with each other. Figs. 11, 13, 14, Pl. V. Some of these branches leave the ducts, and anastomose just outside the trunk from which they are given off. Many of the smaller of these ducts, about the 1-80th of an inch in diameter, have numerous cæcal pouches connected with them, arranged pretty close together. These gradually become shorter as the duct becomes smaller. Figs. 11, 12, Pl. V. The branches springing from these ducts are composed of very thin membrane, often lined with a single layer of epithelium only.

Vasa Aberrantia.—Irregular ducts with cæcal pouches are very numerous in the transverse fissure of the liver, where they form an intimate network connected with the larger branches of the duct in this situation. These were described by Theile as branching mucous glands, but were first noticed and named *Vasa Aberrantia* by Weber. Not only are the right and left hepatic ducts in the transverse fissure of the liver connected by vasa aberrantia, as Weber was the first to point out, but the anastomosing ducts in this situation are so numerous that they form a network, which, in well-injected specimens, presents a very beautiful appearance. Figs. 11, 13, 14, Pl. V. Through the intervention of such branches, all the trunks in the transverse fissure communicate with each other. In the larger Portal Canals, I have demonstrated the existence of numerous ducts of a similar character. In Pl. IV some of these beautiful ducts, with their numerous follicular appendages, from the transverse fissure, are represented. Some observers seem to have altogether failed to demonstrate these curious networks. In every moderately good injection of the ducts, they are seen in great number, but it is not always easy to isolate them, in consequence of the quantity of areolar tissue with which they are surrounded. In order to inject them, it is necessary to force out the bile from the ducts in the first instance, in the manner described at the end of this work. It is difficult to understand how the smallest ducts of a liver could be successfully injected without those of a moderate size being rendered sufficiently distinct.

These ducts are imbedded in areolar tissue, which is abundant in the parts where they are found. In the transverse fissure of the adult, they lie nearer to the hepatic substance than to the coats of the portal vein; but they can easily be removed without cutting into it. I have been able to trace straight ducts from the vasa aberrantia which run directly into the hepatic substance. The further course and destination of such branches is that of an ordinary duct. As far as I can ascertain, such branches as those in the transverse fissures, described and figured by me in my paper to the Royal Society, in 1857, and shown in Pl. IV, p. 48, had not been previously observed. It is, indeed, doubtful whether they could have been made out by the ordinary methods of examination then adopted, for they lie embedded in and obscured by the great quantity of connective tissue existing about the large ducts and vessels in the transverse fissure.

In the fœtus, these curious ducts are much less observable; their course is less tortuous, and they occur in small patches, in which the branches are seen to be very numerous, and the anastomoses very frequent. Figs. 20, 21, 22, Pl. VII. The epithelium is more abundant, and the cells large, and dark in colour; so that the injection does not run so readily as in the adult. The quantity of areolar tissue about them is much less than in the adult. The vasa aberrantia lie so close to the hepatic tissue, that it is almost impossible to remove them without a thin layer of the latter, into which they are prolonged at numerous points. There are, nevertheless, many blind extremities connected with them.

The aberrant ducts connected with ducts of moderate size are, however, numerous in the liver of the human fœtus. Here and there are seen some sacculi, which do not extend beyond the external surface of the coat of the duct. Figs. 20, 21, and 22. The communications between the small lateral and aberrant ducts are so numerous as to constitute an extended network from which here and there branches pass off to the cell-containing network of the lobule. The arrangement is well seen in the figures in Pl. VII, which deserve attentive examination. The coat of the duct is indicated by dotted lines, and the position of the margin of the lobule is also indicated.

Office of the Vasa Aberrantia and Sacculi.—The various facts which have been alluded to, and the arrangement of the structure described in man and animals, appear to me to militate strongly against the notion that the vasa aberrantia are modified and anastomosing mucous glands. They rather point to the ductal nature of these curious channels. I think it not improbable that they are really altered secreting tubes, and at an earlier period of development actually formed a part of the secreting structure of the liver. As the portal vein becomes larger at the termination of intra-uterine life, it is not unreasonable to

INTERLOBULAR DUCTS AND BRANCHES.

Fig. 20.

lobular duct, with parietal sacculi and branches of communication forming a network between the wall of the and the surface of the lobules. Human fœtus. *a* Cell containing network. The tinting shows where the injection had penetrated. *b* Small branch of portal vein with ducts around it. × 29. p. 50.

Fig. 21.

lobu ar duct and branches to cell containing network with fine ches passing to adjacent lobules, showing their continuity with ell containing network in many places, also a few diverticula e coats of the duct well filled with injection. Fœtal calf. × 42. p. 50.

Fig. 22.

From human fœtus. Smaller branches than represented in Fig. 20. × 42. p. 50.

[To face page 50.

suppose that the hepatic tissue, close to it, would recede; the most superficial portion degenerating and becoming so modified, as to be no longer adapted for secretion. The cells would become altered, and many of the ducts shortened and contorted, until a condition such as that figured in Pl. V, Figs. 11, 12, 13, and 14 might at last be produced.

In the very thin edge of a horse's liver, which was composed principally of fibrous tissue, I have been enabled to trace the gradual alteration of the ducts through many intermediate stages to the ultimate complete disappearance of secreting cells, until at length nothing remains but a branched tube without any cells in the interior. The ducts, discovered by Mr. Kiernan in the triangular ligament, in the pons hepatis, and in other situations, are probably produced by a similar change. Fig. 36, Pl. XI.

To the sacculi the office of secreting the mucus which is found in the bile has been assigned by most observers who have investigated this part of the subject, but, from a careful examination of their arrangement, I cannot help doubting the correctness of this inference. Cavities opening into a tube, by a narrow neck often not more than the 1-5000th of an inch in diameter, seem hardly adapted for the secretion and pouring out of a highly viscid mucus. If these so-called "glands" were the seat of the formation of mucus, one would not expect that injections would so readily enter them, and, from their arrangement, it is clear that it would be difficult to force the mucus out of them; again, the complicated and highly tortuous ducts, which Weber termed very properly "vasa aberrantia," possess no characters which entitle them to be regarded as anastomosing mucous glands, a view which has been advocated by Theile. They are most readily injected, and their walls are much thinner than those of ordinary ducts.

It must be remarked that an abundant venous plexus and numerous lymphatics surround the vasa aberrantia (Fig. 10, Pl. IV) and the larger ducts, and it is clear that the bile in the larger ducts, by means of the sacculi, will be brought much nearer to the vessels than would be the case in simple tubes with thick fibrous walls. If these little sacculi were mucous glands, one would be led to expect that the bile of animals in which they were numerous, would be more viscid than that of animals in which they were few in number. I have ascertained that the bile of the rabbit, in which animal these sacculi are almost absent, contains as much mucus as that of the pig, in which they are exceedingly numerous, and are arranged entirely round the ducts. It seems to me that we may regard these appendages connected with the ducts as *diverticula*, in which the bile may be retained temporarily, while it becomes inspissated, and probably undergoes other changes. In fact, I think that we may almost regard them as supplementary little

gall bladders appended to the ducts. In the rabbit and guinea-pig these sacculi are very slightly developed. I have not seen them in the ducts of the fishes and reptiles which I have examined.

Coats of the Larger Ducts.—The coats of the larger ducts are composed of condensed fibrous tissue; but there is reason to think that they contain a few muscular fibre-cells, although there is no evidence of a distinct muscular coat, at least in the human subject. In some fishes an internal layer composed of circular fibres, probably muscular, and an external coat of longitudinal fibres may be demonstrated. Pl. VI, Fig. 19. In the human subject I have observed, but not very distinctly, indications of a somewhat similar arrangement.

Epithelium of the Ducts.—The epithelium of the larger ducts is of the columnar variety. The cells are large and well-formed, usually exhibiting a distinct nucleus. They are frequently tinged with yellow colouring matter, and often contain yellow granules. In the small ducts, this epithelium becomes shorter, and it approaches more nearly to the tesselated variety. This change in the character of the epithelium is a gradual one. In ducts less than the 1-500th of an inch in diameter the epithelium consists of small round flattened granular cells.

The small branches resulting from the division of the trunks in the interlobular fissures, or upon the surfaces of the lobules in the case of the pig's liver, are composed of thin delicate membrane, and are only lined with a single layer of flattened epithelium. In well-injected specimens placed under low powers, these small ducts may, without difficulty, be traced up to the secreting structure of the lobule, but the manner in which they commence, and the relation which they bear to the liver-cells, have long been matters of dispute among anatomists. It has been held by some that the ducts commence by blind extremities on the surface of the lobules; by others, that they are open and impinge against the secreting cells; while, according to the researches of most observers, they commence as very narrow intercellular passages between the liver-cells. This very important question will, however, be fully discussed later on.

GALL BLADDER.

The gall bladder may be looked upon as a diverticulum of the hepatic duct. It lies in a fossa underneath the liver. It is of a pear shape, and its fundus is directed downwards and forwards; it terminates in the cystic duct, which is about an inch in length. The *hepatic* duct, formed by the union of the right and left ducts, leaving the liver by the transverse fissure, passes downwards, and joins the cystic duct at an acute angle, to form the *ductus communis choledochus*, which is about three inches in length, and lies between the layers of the gastro-hepatic omen-

tum. After coming into close proximity with the pancreatic duct, the common duct enters the coats of the intestine with the latter, and passes obliquely between them for three-quarters of an inch. The ducts open by an orifice common to both at the junction of the descending and transverse portions of the duodenum.

The mucous membrane of the gall bladder is highly vascular, and is covered with columnar epithelium. It is thrown into reticulated folds which form the boundaries of numerous polygonal depressions, so that upon its internal surface the mucous membrane presents a honey-combed appearance which disappears or nearly so if the gall bladder is fully distended. The folds are prolonged into the cystic duct, where they are arranged in a crescentic manner, their general direction being that of a spiral, and they no doubt act as has been suggested as a spiral valve. The peculiar arrangement of the vessels of the gall bladder has already been described in page 45. The cystic artery is derived from the right division of the Hepatic Artery, and the veins empty themselves into the Vena Portæ. The lymphatics are very numerous. The greater part of the thickness of the walls of the gall bladder is composed of fibrous tissue, but there also exists a layer, in which muscular fibre-cells, taking partly a longitudinal and partly a transverse direction, are found. The human gall bladder is capable, under ordinary circumstances, of containing about one ounce of fluid ; but it undergoes great alterations in volume, and in it the bile becomes inspissated, and undergoes other changes. Dr. Kemp showed that the mucus of the gall-bladder altered the character of hepatic bile and converted it into cystic bile ; a change which consists not merely of inspissation but of an alteration in chemical composition.

The gall bladder can hardly be regarded as a necessary viscus, since it is absent in many instances in which its absence cannot be accounted for by peculiarities in the food of the animal. The fact of the accumulation of bile in the gall bladder in the ox and sheep for example, and its non-accumulation in the horse, is remarkable. This viscus, is absent in many fishes ; in pigeons, toucans, and some other birds ; in the elephant, stag, horse, and tapir ; but it is present in the ox, sheep, and antelope. It is always found among reptiles.

No one can study the general arrangement and course of the large and moderate sized ducts of the liver of man and animals, without being struck with the frequent communications and anastomoses not only between the ducts of various sizes, but between the diverticula and lateral extensions of individual ducts. The inspissation of the bile effected by this arrangement is sometimes carried too far, and occasionally the process goes on until hard masses are formed which cannot pass along the ducts. These sometimes become so firm and hard that they and their ramifications when detached, look not unlike

the twigs of a tree. Small pieces of inspissated biliary matter forming a mould of a portion of a duct are not uncommon. But though the obstruction of a portion of the duct be quite complete, the bile passes into ducts beyond the point of obstruction and reaches the pervious portion through the numerous communicating channels. Pls. V, VII.

NERVES.

The nerves of the liver are branches from the pneumogastric and the sympathetic, are principally distributed upon the artery, and the mode of their arrangement is very similar to that of other arterial trunks. Although the coats of the larger ducts contain little contractile tissue of any kind, nerves are distributed to them, and fine nerve-fibres ramify in the substance of the coats. The coats of the finer gall ducts certainly contain no muscular fibres whatever. Nevertheless, dark-bordered and fine nerve-fibres ramify over them, and even in the frog and newt I have demonstrated fine nerve-fibres in close relation with small thin-walled ducts. Perhaps as regards number, there may be nearly a fourth as compared with the number distributed to small arterial branches. The nerve-fibres in question are, no doubt, afferent in their action, and probably have to do with the regulation of the supply of nutrient matter by their indirect influence upon the calibre of the nearest arterioles. They correspond indeed in distribution and action with the networks of fine nerve-fibres distributed to fibrous tissue.

The finest nerve-fibres which form a lax network around the uriniferous tubes can be very clearly demonstrated in the thin thoracic portion of the newt's kidney. These are represented in Fig. 15, Pl. V, p. 48. At intervals are seen oval masses of bioplasm, the so-called nuclei. In the liver of the frog and toad I have seen a precisely similar arrangement, but it is only to be demonstrated in exceptional cases, where a very thin divergent layer of hepatic tissue can be found projecting either from some part of the circumference of the liver, or extending into some of the fibrous extensions or ligaments, or in some of those partly wasted portions of hepatic tissue met with near the entrance of the large vessels in the transverse fissure. I am convinced that none of the fine nerve-fibres are connected with the hepatic cells, and feel confident that the instances in which a dark-bordered nerve-fibre has been followed up to the cell are errors of observation. The very fine fibres I have demonstrated are clearly seen in specimens mounted in glycerine, and there is no difficulty whatever in following dark-bordered nerve-fibres for long distances till, after becoming very gradually thinner, they are at last seen to end in the network of the very fine fibres described and figured.

LYMPHATICS.

The lymphatics are abundantly distributed to the liver. Plexuses are found in the capsule on the surface, in the transverse fissure in the portal canals, and on the surface of the gall bladder. Many unsuccessful attempts had been made to inject the lymphatics of the liver, before the plan which ultimately succeeded was adopted. I had been able to force injection for some distance along the larger trunks in the opposite direction to that in which the valves opened, but could not obtain satisfactory injections of the smallest vessels. The largest lymphatic vessels in the portal canals are often injected by rupture of the coats of the duct, and by extravasation of the injection, as Mr. Kiernan remarked in his paper. The same thing has many times occurred to myself, but under these circumstances the injection always runs towards the transverse fissure, in the direction which the arrangement of the valves permits the fluid to pass readily, and the smaller branches of lymphatics are never injected.

The drawings in Pl. VIII were obtained from preparations which were made as follows: an ox liver was thoroughly injected with warm water from the portal vein, as if the ducts were to be injected; gradually the organ became distended, and much fluid returned by the lymphatic vessels. Many large trunks running over the surface were in this way fully distended with water. Into one of these swollen trunks a small pipe was inserted with much difficulty, and the vessel was tied round it. The whole organ was wrapped up in cloths and subjected to considerable pressure for upwards of twenty-four hours. When the water had been absorbed, the lymphatic vessels were quite invisible, and it would have been impossible at this time to have found a trunk into which a pipe could have been inserted. A little of the Prussian blue injecting fluid was now forced into the pipe from a small syringe. It passed for some distance along the trunk of the vessel, and by pressing the large trunks a little from time to time, the injection was made to pass the valves, and forced into the smaller branches. By using slight but gradually increased pressure, the trunks were so distended as to prevent the meeting of the valves. In the course of half an hour or longer, an abundant network of lymphatics upon the surface had been fully injected, without any extravasation. Fig. 23, Pl. VIII It was now considered desirable to wait awhile, before introducing more fluid. After a few hours the injection was resumed until as much fluid had been forced in as could be introduced without running the risk of rupturing the vessels. I have tried the same plan with the human liver, but hitherto with imperfect success. The trunks are much smaller, and their walls are more delicate than those of the liver of the ox.

After the lymphatics had been injected as above described, thin pieces were removed for microscopical examination. Upon taking thin

sections from the surface it was discovered that the injection had passed into many of the lymphatics of the portal canals, not only into the canals lying just beneath the capsule, but into some situated at the depth of an inch or an inch and a-half in the substance of the liver.

The general arrangement of the larger lymphatic trunks, the free communications between the superficial branches on the surface and the deep ones in the substance of the liver, and the course of the larger branches towards the thoracic duct, have been fully described in Quain's Anatomy and other works, and it is, therefore, unnecessary to discuss this part of the subject.

The lymphatics used to be injected with mercury, and although this process was well adapted for showing the course of the larger trunks, the great distension produced rendered it impossible to ascertain the arrangement of the smaller vessels, even supposing them to be injected : but the materials employed by the older observers seldom penetrated into the smallest branches. The appearances delineated in the accompanying drawings, Pl. VIII, Figs. 23 to 26, could only be obtained where a transparent injecting fluid had been employed, so that the specimen could be examined by transmitted light.

The network represented in Pl. VIII, Fig. 25, really occupies several different planes, and lies partly in the substance of the fibrous capsule of the liver, and partly immediately beneath this structure. The smallest vessels have been injected, though in many situations not quite perfectly. There can, I think, be little doubt that the smallest branches form an intricate network. I have not been able to demonstrate the existence of blind extremities, although I am not in a position to assert that lymphatic vessels never commence in this manner. In Fig. 25, some very narrow branches are represented, many not being more than 1-2000th of an inch in diameter. In the preparation from which this drawing was taken, a network is seen in many places, the branches of which do not absolutely communicate, though in many instances they are exactly opposite each other, a circumstance which renders it more probable that the tube in the interval is uninjected, than that there are cæcal tubes lying in juxtaposition. The point at which the injection ceases is ragged, and of the same diameter as the rest of the tube, while if there were commencing blind extremities, they would be rounded, and probably a little wider than the rest of the tube.

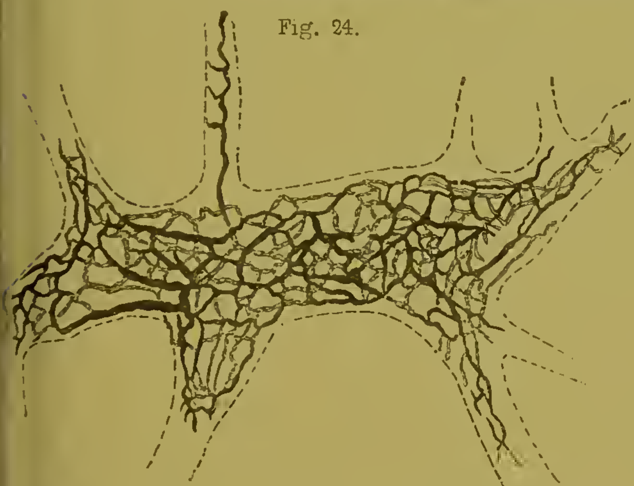
In many places the injection had accumulated in front of the valves, and had distended the tube very much, as represented in Fig. 25, Pl. VIII. In Fig. 24, from a portal canal, the injection is perfect, although doubtless the tubes are distended beyond their natural extent. Here, evidently, there is a network entirely surrounding the vessels contained in the portal canals, and on either side of the large canal

LYMPHATICS OF THE LIVER.

Fig. 23.

rtion of the plexus of lymphatics running in the capsule on the convex surface of the liver of the ox. The smaller branches are destitute of valves. × 40. p. 55.

Fig. 24.



phatics from a portal canal of the liver of the ox. Several small ranches are seen passing along the smaller canals. × 15. p. 55.

Fig. 25.

A portion of the network represented in Fig. 24, more highly magnified. × 215 p. 55.

Fig. 26.

One of the smallest branches of lymphatic vessels, injected, showing position of the valves. × 215. p. 55.

[To face page 56

smaller ones are observed to pass off. These small canals also have their lymphatic vessels. No blind extremities can be found here, and if they existed, I think at least a few would be distinguished in a part of the preparation where the injection is evidently very perfect.

In some places injection has passed from the branches in the portal canal to some distance within the lobule, and, as far as I can make out, it lies in spaces between the capillaries and the cell-containing network. There is no evidence of extravasation, and the appearance precisely accords with what one would expect to find if the above view were true.

Function of the Lymphatics.—There is no reason to suppose that the action of the lymphatics in the liver is in any essential respect different from their action in other tissues and organs, and it is probable the lymph corpuscles take up excess of certain nutrient materials and restore these to the blood. Under certain circumstances the lymph corpuscles grow and multiply enormously, and the process results in the formation of collections around the tubes of the cell-containing network, pressing upon the liver-cells and ultimately interfering with their action and growth. In the same manner the germs of cancer-cells may be distributed, and may ultimately cause complete destruction of the hepatic cells, with obliteration of these and the other elements of hepatic structure. In disseminating bacteria and pus the lymphatics are instrumental, and in some of the lower animals branches may be found which are completely distended with bacteria, the arrangement of the lymphatic network being thus rendered distinct.

HEPATIC VENOUS CANALS.

The other series of channels which can be traced from the deep oblique notch on the posterior thick border of the liver contain branches of the hepatic vein, and every part of the liver is brought into an equally close relation with one of these canals, which have been termed by Kiernan *Hepatic Venous Canals.* Pl. IX, Fig. 28, p. 64. Such is the arrangement by which the vessels are brought into close relation with every portion of a very large and compact gland. By it an equable distribution of the blood to each individual part is insured, while the capillary vessels of the lobules very near to the large vessels are not subjected to a stronger blood pressure than those which are far distant, and in cases of varying blood supply within the healthy range, all danger of undue congestion of the capillaries is averted.

HEPATIC VEIN.

The radicle of the hepatic vein (intralobular) is always seen at a point midway between branches of the portal vein, and in the centre of each of the distinct lobules in the case of the pig.

If the trunk of an hepatic vein of moderate size be laid open, the openings of numerous small veins will be observed upon its interior, about one-thirtieth of an inch from one another, *b*, Fig. 28. These openings correspond to the centres of the lobules which are nearest to the trunk of the vein, as described by Kiernan. It is by reason of the entrance of these minute intralobular branches into the large trunk of the vein, that the latter remains patent when cut across.

The capillary meshes are elongated as they approach the hepatic vein, and they converge towards this vessel, the smallest trunk of which is much larger than the smallest branch of the portal vein. The small radicles of the hepatic vein receive capillaries on all sides, quite down to the point where they emerge from the lobule; and these small intralobular veins, in many instances, open, not into a vessel somewhat larger than themselves, but pour their blood at once into a large trunk. In these points the arrangement of the hepatic vein contrasts remarkably with that of the branches of the portal trunks, and the reason of the difference is clear. In no other manner, consistent with the compact nature of the mammalian liver, and without loss of space, could portions of the portal blood be equally distributed, and made to pass through the extensive capillary system existing in the thousands of lobules which constitute the liver. After having passed through the extensive lobular capillary plexus, the blood is poured into the intralobular branches, and carried away from the liver in the most direct manner possible. Occasionally an anastomosis takes place between the small branches of the hepatic vein. One of the most remarkable I have seen occurs in a preparation taken from the human liver.

Hepatic Vein in the Seal.—In the seal the capacity of the branches of the hepatic vein within the liver is enormously greater than in other animals, an arrangement which has reference to the accumulation of blood in this organ, and in the great venous sinus into which the trunk of the hepatic vein is dilated when the animal remains for some time under water. Accumulation of the blood, in the small branches, to an improper extent, is prevented, while its further progress towards the hepatic venous sinus, after its accumulation, is promoted by a beautiful arrangement to which I must briefly refer. The peculiarity in question was first noticed by Mr. Kiernan, who described the external coat as consisting of circular fibres. In the smaller trunks these fibres are arranged in the form of circular fasciculi, external to which is a certain quantity of lax areolar tissue, which permits of great alteration in the volume of the veins taking place. When the hepatic veins were injected with plain size, I was surprised to find that a beaded appearance was produced. The actual specimen was shown in my lecture on the Liver at the Royal College of Physicians in 1862. Upon making a longitudinal section of a small branch of the vein which had been

injected, it was seen to be partially divided into a number of small chambers, by means of septa, which were well shown in the preparation. At the situation of each partition a circular band of muscular fibre-cells, which is enclosed at intervals in the lax fibrous coat, may be very easily demonstrated. It is no doubt the office of these contractile circular partitions to prevent undue distension, to equalize the accumulation of blood in the branches of the vein, to drive it onwards towards the cava, and to prevent undue pressure upon the secreting structure of the lobule.

I know of nothing in any other animal at all resembling this very remarkable arrangement of the circular muscular fibres of the venules. Sacculated venules and irregular dilatations connected with small veins are not uncommon, but the arrangement here pointed out is remarkably regular, and must subserve some very important purpose in the economy of the liver of this particular animal.

In temporary derangements of the circulation in which a large proportion of the blood of the body is caused to leave the vessels of the surface and accumulate in the internal organs, the several subdivisions of the hepatic vein no doubt receive a considerable amount. It is probable that when the accumulation occurs very frequently, the branches become dilated, while the pressure exerted upon the lobular tissue causes it to yield, and as time goes on the growth and multiplication of the cells which take place chiefly in the central parts of the lobule are impeded. In some cases probably the change in question goes to the extent of entirely checking the growth and multiplication of the cells, and of at last destroying all those that have hitherto withstood the pressure and attending conditions so adverse to them. In this way what was first but an oft-repeated physical disturbance, at last results in serious structural change which may eventuate in gradual wasting of the organ and at last cause the patient's death.

OF GLISSON'S CAPSULE AND OF THE MAPPING OUT OF THE LOBULES OF THE LIVER.

This structure, since the time of its discoverer, has been described as a most important and essential constituent of the liver. Continuous with the proper capsule of the organ externally, it is said not only to form a sheath for the large vessels as they lie in the portal canals, but to be prolonged with them into the ultimate parts of the gland, and even to form for each lobule a proper investment, or, as others have described it, a partition between contiguous lobules.

As a protecting and supporting framework to very soft and delicate

structure Glisson's capsule has been regarded a necessary anatomical element.

One of the most common, as well as perhaps the most commonly fatal of all forms of hepatic disease, *Cirrhosis*, has been attributed to inflammation of this so-called Glisson's capsule,—this connective tissue which invests the liver and has been described as prolonged into every part of the substance of the gland, mapping out the organ as it were, into a great number of elementary livers, and constituting the boundary and limit of each portion or lobule. In that form of inflammation known as cirrhosis, this low form of connective tissue is said to be inflamed and then to undergo slow contraction and condensation, whereby the more important structures of the liver are constricted or compressed, and their action impaired. This chronic process ends at last in complete degeneration, the whole organ shrinks in size, and is almost reduced to a mass of passive scarcely changing fibroid tissue.

Facts, however, as I shall endeavour to show, render it necessary to regard this structure from a very different standpoint, for in the liver of young small animals not a vestige of this Glisson's capsule can be demonstrated between the lobules, and it is more probable that the capsule itself results from degenerative changes in the superficial lobules at a very early period of development than that it is specially developed or a distinct tissue for a particular purpose. In the human embryo scarcely a trace of any tissue can be found in the interlobular spaces, but as age advances it makes its appearance, while in old age the amount of this tissue is very considerable. In disease, as already mentioned, it may become abundant even at a comparatively early period of life.

It is an important point to ascertain whether the arrangement of this connective tissue of the liver presents any special characters and differs as regards its structure and mode of formation in any very essential particulars from that of other glandular organs. Mr. Kiernan pointed out that, in the smaller portal canals, Glisson's capsule did not completely "invest" the vessels, but was only to be found upon that side of the vein on which the duct and artery were situated. Anatomists have failed to demonstrate a trace of connective tissue within the lobules of the liver between the vessels and the secreting structure. Occasionally, a few fibres of a structure like fibrous tissue may, undoubtedly, be observed in uninjected specimens; but the fibrous appearance is generally proved to be due either to physical alterations in the structures of the lobule, effected by the method of preparing the specimen, or to disease. In the lobules of the livers of all the animals which I have examined, no fibrous structure whatever could be demonstrated in the situation referred to.

Even in the *interlobular fissures* of the perfectly healthy human

liver of a child, and in the liver of animals allied to it in structure, very little fibrous tissue of any kind exists, but as age advances there is no difficulty in demonstrating fibrous structure. No true areolar tissue exists in the smallest portal canals and interlobular fissures of the human liver.

On the other hand between the capsule of adjacent lobules in the pig's liver, a very delicate form of fibrous tissue undoubtedly exists. The "capsule" of the lobule can in fact be easily demonstrated, for its contents can be washed out. It is composed of exceedingly fine fibrous tissue quite distinct from the areolar tissue found in the large portal canals. In the latter situation the ordinary elements of areolar tissue, white and yellow fibrous tissue, and not unfrequently adipose tissue, are met with. It will, however, be pointed out in what important particulars the arrangement of the lobules of the pig's liver differs from that of other animals.

In the human liver in early life, although there is a considerable quantity of areolar tissue surrounding and adhering to the large vessels, at the point where they enter the liver, and in the larger portal canals, this gradually becomes less, and is, at last, almost lost as we approach the smaller portal canals, but in old age this tissue is abundant.

The amount of this connective tissue (Glisson's capsule) in the large portal canals varies very much in different animals. In rodent animals generally, it seems reduced to a minimum; in the seal it is very sparing in quantity, but in the young white mouse there is scarcely a trace to be found even in very thin sections, specially prepared for the purpose of demonstrating its arrangement.

Structures which may be mistaken for Fibrous Tissue.—Embedded in the connective tissue present in such large amount in the portal canals of the adult human liver are many structures which cannot be recognised in specimens submitted to ordinary examination, and all of which are mistaken for and included under the head of "*interlobular connective tissue*" or "*Glisson's capsule.*" Among the definite structures are:—lymphatics, nerves, vessels, branches of the ducts, and vasa aberrantia, all of which have been included under the head of Glisson's capsule.

In the horse, the external coats of the large duct and portal vein are incorporated at the point where they touch, and here the areolar tissue clearly belongs to the external coat of these vessels. In the rabbit very little connective tissue is found to accompany or invest the vessels of the liver. If the vessels of the rabbit's liver be injected with plain size, the whole organ becomes transparent, and the course of the small distended veins can be most easily traced in specimens magnified from twenty to forty diameters. In this animal the capillaries of the liver are large, and injection runs into them very readily. One cannot fail to be struck by the almost total absence of anything which can be

described as Glisson's capsule, or fibrous tissue, in this beautiful liver. A little condensed areolar tissue is seen only around the largest veins, and external to it ramifies an abundant plexus of lymphatics. In sections showing portal canals all the vessels are seen to be clear and well-defined. The artery can be readily separated from the portal vein, and certainly neither it nor the duct can be said to be bound up with the vein in a fibrous sheath. The larger ducts can be readily distinguished from the other vessels, and their small branches, if not injected, can be traced for a long distance by the characteristic epithelium in their interior. In the smaller portal canals the veins and ducts are destitute of any external coat, but their course may, nevertheless, be followed without much difficulty.

When the ducts of a liver (human, rabbit, seal, and other animals) have been injected with Prussian blue, and the portal vein distended with plain size, a transverse section of a small portal canal exhibits little of a structural character besides the distended veins and ducts, with branches of the artery. The external coat of very large veins may be well seen consisting of a thin layer of condensed areolar tissue ; but the duct and artery are not invested with the latter. In the small portal canals the vein is quite destitute of this external coat, and it lies in immediate contact with the basement membrane of the peripheral portion of the cell-containing network, or with the finest ducts, which often form a plexus around it. In a transverse section of a portal canal of the seal's liver, the smaller ducts, of which a few branches only are very imperfectly injected, may be seen passing round the artery and portal vein. These small ducts in many preparations seem to enclose the artery and duct, in a network like a sheath, and this in uninjected specimens seems to be connected with the coat of the portal vein, but the real nature of this apparent sheath is clearly shown in many specimens which I have prepared and of which drawings have been made. There is in short, no doubt that in many cases the shrunken vessels and fine ducts which in my specimens have been injected have in their uninjected state been mistaken for fibrous or connective tissue.

The difficulty of deciding positively upon this point, in some specimens submitted to examination, is, however, greater than would be supposed from the remarks I have just made ; for although by manipulation the small vessels in uninjected specimens become so altered that it would be impossible to distinguish them from fibrous tissue, it might be urged on the other hand, that in injected specimens the fibrous tissue is so compressed by the distended vessels that it has become almost invisible ; but even in this case, in numerous places where these vessels are slightly separated from each other, one could hardly fail to recognise fibrous tissue if it existed.

The areolar coat of the larger vessels and ducts is not prolonged upon the small branches which are given off from the ramifications in the larger portal canals; and, after many careful examinations of the arrangement and connexions of the vessels in the portal canals of many animals, I have been unable to observe anything in the distribution of the areolar tissue around the vessels of the liver differing from its arrangement in other glands. The vessels of the kidney for instance, as is well known, are invested at their entrance, like those of the liver, with much areolar tissue, which is gradually lost as the vessels approach the secreting portion of the organ.

Manner in which the mapping out into distinct portions is produced.— The cause of the mapping out of the lobules of the liver in all animals has been considered to be due to the extensive distribution of Glisson's capsule between them; but in these situations, as has been already remarked, many observers like myself have altogether failed in their attempts to demonstrate such a structure, with the single exception of the pig. The fibrous appearance in the interlobular spaces of the un-injected livers of animals generally, I have shown to be due to the collapsed state of small branches of the vein, artery, and especially of the duct, which are very numerous. As far as I am able to judge, many authorities have entertained the opinion that Glisson's capsule was developed as a special structure, and discharged a special office, and was as much an integral and necessary part of hepatic structure as the cells or the vessels. This view is not, however, supported by the observations above referred to.

The divisions, or apparent septa, between the ultimate portions of hepatic substance in the human liver (independent of alterations in vascular distension so well described by Kiernan) seem to be produced in part by the arrangement of the smallest branches of the duct, and partly by that of the vein and artery. See Pl. I, p. 38. In the seal and hedgehog the markings are not very distinct, and the ducts passing to the lobules are few in number, and have a short and simple course. In the frog and newt, and in fishes generally, the markings held to indicate the divisions into lobules are very indistinct, and there is no regular arrangement of small ducts round portions of hepatic tissue similar to that which exists in mammalia. In the uninjected state, and without previous preparation, these small ducts are so stretched and torn by manipulation that it is impossible to distinguish the striated appearance from that characterising ordinary fibrous tissue.

The boundary lines which seem to intervene between the lobules of the human and other livers, as seen by the unaided eye, are, in the majority of cases, due to a difference between the cells at the surface of the lobule close to the ducts, and those in the interior. In the former situation the cells often contain many oil globules, which are

white by reflected light, and appear like a distinct line of separation, while in the latter they frequently contain colouring matter alone.

The small ducts which have been referred to in the last paragraph have been represented in Fig. 33, Pl. X. Although numerous branches have been successfully injected in the preparations from which my drawings have been taken, I feel convinced that, from an examination of such specimens alone, a very imperfect idea would be formed of the vast number of these finest ducts existing in the interlobular fissures of a healthy liver.

In the human fœtus, the separation into lobules is very distinctly marked, but the appearance is not due to the presence of a fibrous capsule, or to the existence of fibrous tissue; for in a well-prepared specimen every portion of space between one of the lobules, or spaces mapped out, and its neighbours, can be seen to be occupied with branches of the vein, artery, and duct, which may be injected. In such a preparation the complete absence of any structure like fibrous tissue is very remarkable.

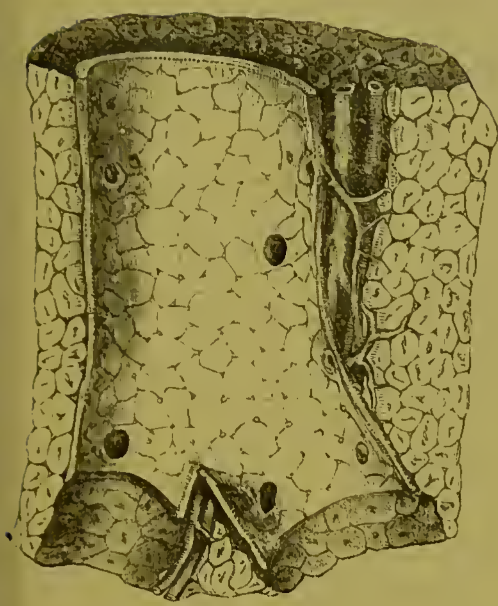
The mapping out then is really produced in many cases by the different appearance of the central and circumferential part of the little elementary portions of liver. The first are usually more or less coloured, while the intervals between these coloured portions are colourless or nearly so. In these intervals the portal vessels and duct reach the circumference of the lobule, and become continuous with the capillaries and cell-containing network of which the secreting structure is composed.

The "interlobular spaces" are apparently increased in extent in certain cases of disease where the liver-cells at the margin of the lobule have degenerated. This increase, of course, takes place at the expense of the secreting structure of the lobules, which in a section are seen to be much diminished in size. I have specimens of diseased liver in which the so-called "interlobular spaces" are as wide as the "lobules." That this is due to an alteration in the secreting structure of the lobule is certain, because the network which originally contained liver-cells can be distinctly traced (Pl. II, Figs. 4, 5, 6, Pl. XI, Figs. 39, 40), and in many situations exhibits biliary particles. Such a specimen would have been formerly described as produced by thickening of Glisson's capsule. The interlobular spaces then are occupied only by branches of the vessels and duct which lie in close proximity to each other, and no structure corresponding to the description given of Glisson's capsule is to be detected in this situation.

With reference to the physiological arrangement of the elementary tissues of which the gland is composed, it may, I think, be said that the livers of all vertebrate animals are physiologically arranged in small more or less isolated portions, or *lobules;* but in a strictly anatomical sense, the term can only be applied to the lobules of the liver of the

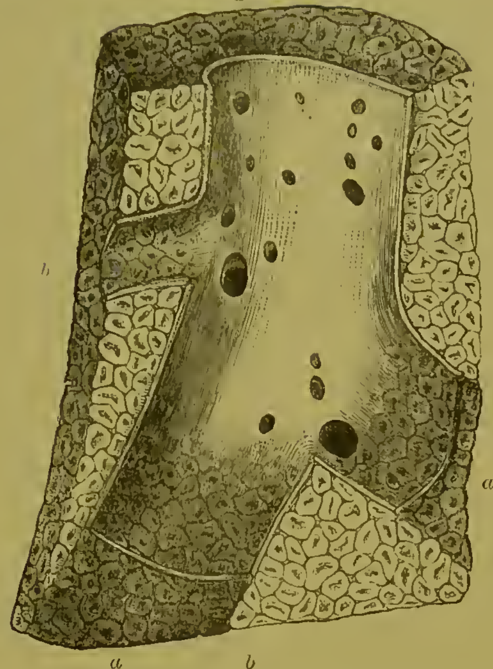
FIGURES FROM KIERNAN'S MEMOIR.
1833.

Fig. 27.



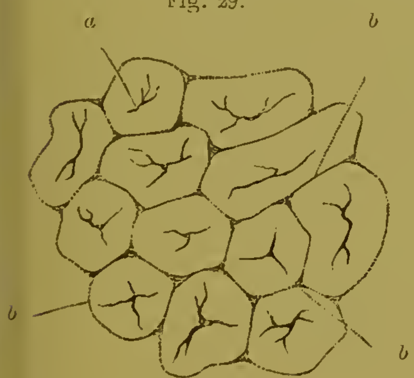
Longitudinal section of a small vein and canal The artery and duct are seen on the right of the vein. Kiernan. p. 38.

Fig. 28.



Longitudinal section of hepatic vein. The walls of the vein have been removed at *a*, *a*. *b* Sublobular hepatic veins opening into trunk. Kiernan. p. 57.

Fig. 29.

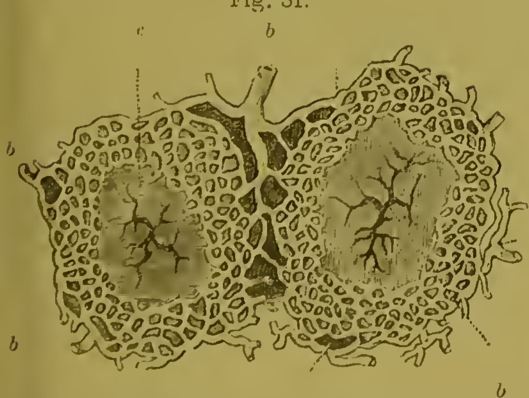


Lobules as they appear in a state of anæmia. *a* Intralobular veins. *b* Interlobular spaces and fissures. Kiernan. p. 65.

Fig. 30.

Lobules in a state of hepatic venous congestion. *a* Congested intralobular veins and capillaries in central part of lobule. Kiernan. p. 65.

Fig. 31.



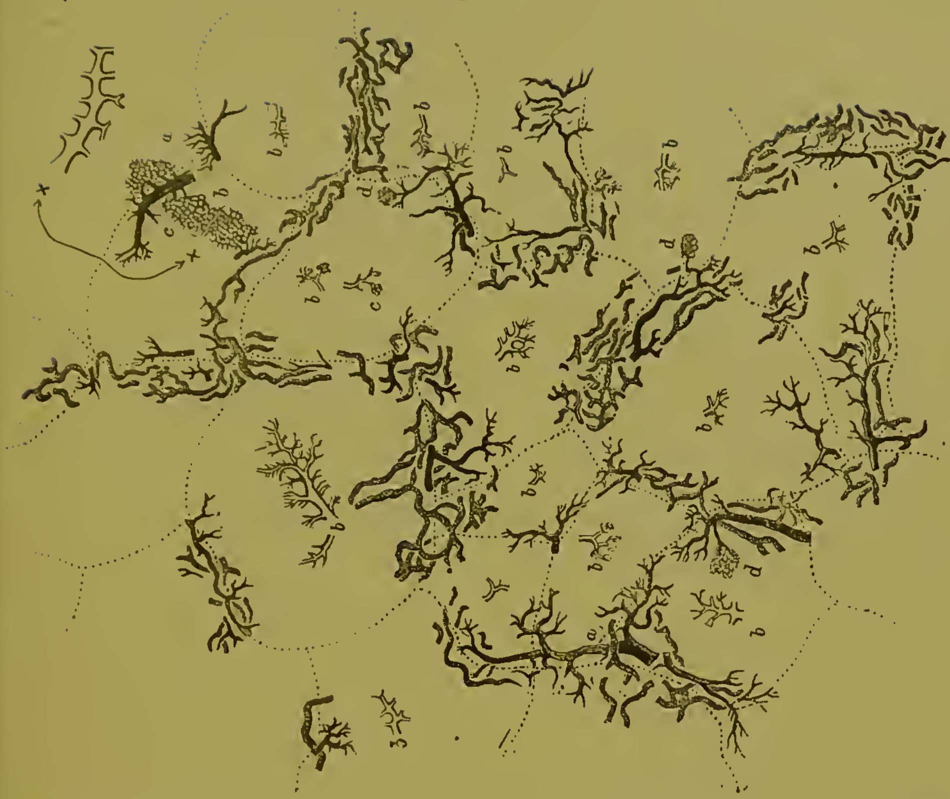
Interlobular ducts entering the lobules and forming the lobular biliary plexus. *b* Interlobular ducts. *c* Central part of lobules uninjected, with branches of hepatic veins. Hypothetical. Kiernan. p. 6.

Fig. 32.

Lobules in portal venous congestion. *a* Intralobular veins containing no blood. *b* Portal capillaries congested. Kiernan. p. 65.

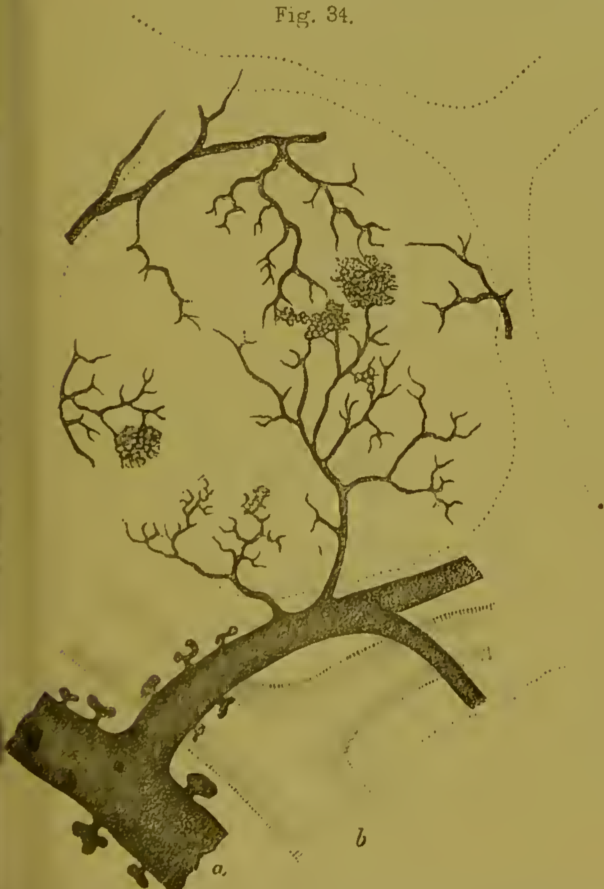
[To face page 64.

Fig. 33.



Thin transverse section of human liver showing the ducts in the interlobular fissures. The branches of the portal vein are black in the drawing. × 15. p. 64.

Fig. 34.



A very small lobule of the pig's liver showing the ducts dividing into branches on the surface of the capsule. In one or two places the injection has run into the cell containing network. *a* Duct with diverticula injected. *b* Branch of interlobular (portal) vein. × 42. p. 48

L.S.B

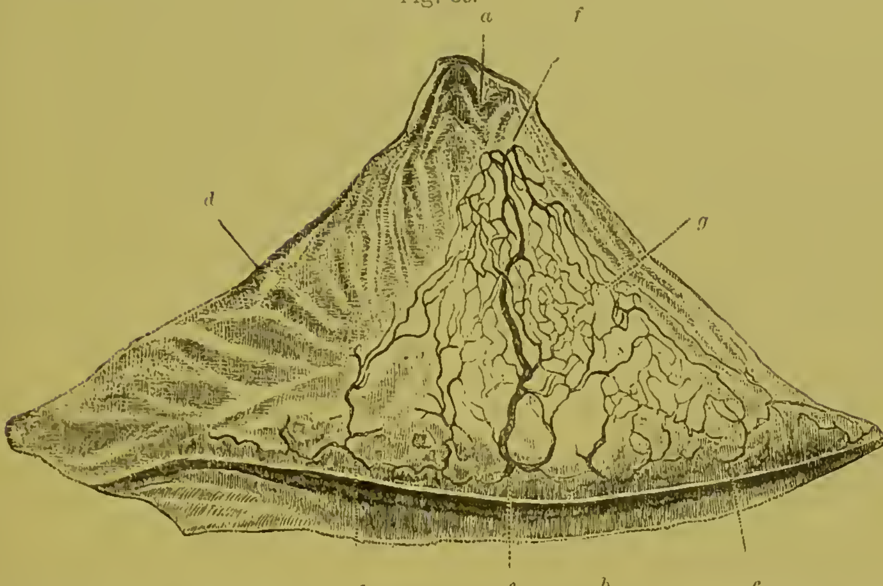
Fig. 35.

A small duct dividing on the surface of the lobule with injection of portions of the cell containing network. × 42. p. 48.

[To follow Plate IX.

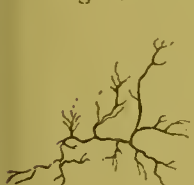
FINEST DUCTS AND ALTERED CELL—CONTAINING NETWORK.

Fig. 36.



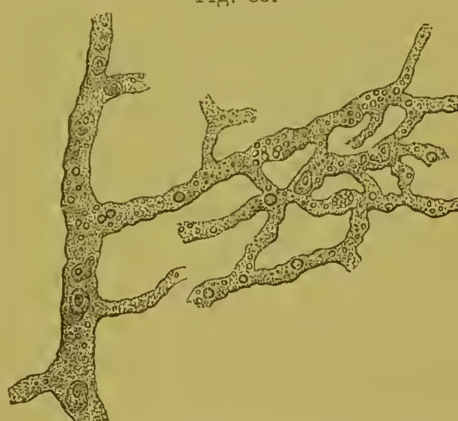
The biliary ducts ramifying in the left lateral ligament of the human liver. *a* Left lateral ligament. *b* Posterior edge of left lobe *c* Loose edge of ligament. *d* Edge connected with diaphragm *e e* Biliary ducts from liver ascending to ramify in the ligament. Arches formed by ducts. *g* Network of small ducts. Kiernan. p. 51

Fig. 37.



Ducts of lophius piscatorius injected. Natural size.

Fig. 38.



Cell containing network just on the surface of a lobule of the liver, showing small cells which probably are not active in secretion. × 215. Pig

Fig. 39.

Cirrhosed liver, showing the wasted tubes of the cell-containing network of the outer parts of the lobules. Human. × 20.

Fig. 40.

Wasted tubes of cell-containing network from outer part of lobule. Same specimen as Fig. 39, but × 215

[To follow Plate X.

pig, since it is only in this animal that individual lobules can be separated from one another.

LOBULES OF THE LIVER.

If the surface or a carefully made section of a liver be examined, it is perceived to be mapped out, as it were, into a number of little spaces, about the size of a millet seed, but differing slightly from each other in dimensions and form. The appearance of the markings is different in the livers of different animals. In the pig each little portion of tissue is circular, oval, or polyhedral, and is completely circumscribed, but in the human subject they are elongated and less definite in form, and seem to fit into, or in a manner to dovetail with, each other. In other mammalian animals the markings are more or less distinct than in the human subject, but in no one are these spaces defined in the distinct manner in which they are in the pig. If a section be made in various directions in different parts of the organ, a similar mapping out is seen, although, perhaps, it is not quite so distinct as upon the surface. The structure of all these little component masses of the liver is similar. The whole liver is composed of an immense number of these small portions of hepatic tissue resembling one another. Each little mass, whether it be perfectly circumscribed, as in the pig, or less completely so, as is the case in other animals, is termed a "lobule." A lobule, then, contains all the essential elements for the secretion of bile, and for effecting those changes in the blood which this fluid is known to undergo in its passage through the capillary vessels.

Each lobule comprises all the hepatic elements and may be regarded as a small elementary liver. The entire organ is a collection of lobules, and the large liver of the elephant differs from the small liver of the mouse enormously with respect to the number, but only very slightly as regards the size, of the component lobules.

Lobules of the Pig's Liver.—Now, the individual lobules are most perfectly seen in the pig's liver, and also in that of the Polar bear, according to Müller, and in that of the *Octodon Cummingii* (one of the rodents), according to the observations of Hyrtl; and these livers in their anatomical arrangement differ vastly from those of other animals with which I am acquainted, as regards the separation of the lobules from each other. With care, a portion of the liver of the pig may be separated into a number of small roundish masses, like very small seeds, Pl. IX, Figs. 27 to 32. Each is invested with a firm, fibrous membrane of its own, indicated by a dotted line in Fig. 34, Pl. X; and, if it be pressed strongly, it bursts, and its contents may be squeezed out. Upon the surface of this lobule ramify small twigs of the *portal vein*,

hepatic artery, and *hepatic duct;* many branches from these perforate the capsule at various points, and are distributed *in the interior of the lobule.*

The capsule of the lobule of the pig's liver is composed of a form of fibrous tissue. The fibres are exceedingly delicate, and so arranged as to bound small apertures, through which branches of the vessels and duct pass to the interior. The capsules of adjacent lobules are connected together by the branches of these vessels, and, in many instances, by a small quantity of fibrous tissue.

Many observers describe the lobules of the pig's liver as being surrounded with an expansion of the capsule of Glisson, an arrangement which is sanctioned by Kölliker, who considers that the fibrous material forms partitions between the lobules instead of forming a distinct and separate capsule to each lobule, but his view is not accurate. If a piece of fresh pig's liver be injected from the portal vein with alcohol, to which a few drops of a solution of soda have been added, and then the whole soaked in the same solution for a few days until it has become hard, the lobules can be readily separated in the manner above described. In very thin sections, from well prepared specimens in which the vessels have been injected, the separate outlines of the capsules of adjacent lobules may be distinctly seen; there is an interval between them in which the vessels lie. I have some preparations in which this point is very clearly demonstrated.

At one particular spot, and here only, a small twig of the hepatic vein perforates the capsule, and receives on all sides the capillaries from the interior of the lobule, which converge towards this small central or intralobular vein. If the hepatic vein be injected, and the lobules separated from each other to a great extent, but left attached to the small branches of the vein, they would seem to be arranged upon the terminal branches of the vein, Pl. IX, Figs. 29, 30, almost like leaves upon their leafstalk. In attempting partially or completely to isolate the lobules from each other, the branches of vessels distributed upon their surface are, of course, much torn, since, in all instances, the vessels conducted to the lobules in the portal canals (*portal vein*, *hepatic artery*, and *hepatic duct*) are *interlobular*, that is, run between the lobules, and give off branches to those among which they pass, as they pursue their somewhat tortuous and irregular course. Such is the anatomical arrangement and connection with each other of the small circumscribed portions of hepatic tissue of the liver of the pig and Polar bear. The entire organ is built up of a number of elementary masses connected with each other, not by continuity of the capillary vessels, or of the secreting structure of the lobule, but only by the vessels for their supply, and by a little areolar tissue connected with these vessels. This separation into lobules serves to give a certain compactness to the entire

organ as a whole, while at the same time it allows great alteration in volume, with a certain mobility between each of its elementary parts As regards the liver of the pig, the very free movement of the lobules upon their neighbours which is provided for by the arrangement in question has reference to the very considerable alteration in volume the organ undergoes within a short period of time, consequent upon the gorging habits of the animal. Each lobule may increase in size without compressing or stretching the fine branches of the vessels and ducts between it and neighbouring lobules. The degree to which the healthy liver of the pig may be temporarily enlarged is very remarkable. The organ will easily contain a quantity of water equal to its own weight, which may be injected from the portal vein; and its lateral and antero-posterior dimensions will be increased as much as two inches each way; while, although, by using great force, almost as much fluid may be forced into the human liver, it only increases from half to three quarters of an inch in the same directions.

In other animals it is impossible to isolate the elementary parts of the organ from each other without leaving a very rough and jagged surface. When this isolation is attempted, the surface of the little masses seems to be rough and uneven; their form is irregular, they have evidently been torn. The true secreting portion of the gland is injured in the attempt. In fact, the secreting structure and capillary plexus of one imperfectly isolated portion of hepatic substance is at certain points continuous with the corresponding elements of the neighbouring lobules. The general arrangement of the vessels, however, is essentially the same in all cases. When the lobules are provided with a separate capsule, as in the pig, the portal vessels ramify upon their surface; but, when they are not thus isolated from each other, the vessels penetrate into the substance of the lobule at tolerably regular distances, lying in channels or interlobular fissures. Sometimes the fissures are flattened and of considerable width, while, in other instances, they may be compared to tubes separated from each other by a certain interval, in which the capillary vessels, and secreting network, of one lobule communicate with those of its neighbours.

The Lobules of the Pig's Liver compared with the Renules of the Kidney of the Porpoise.—The distinct and elementary lobules in the pig's liver may be looked upon as exceptional, and the liver of this animal appears to bear the same anatomical relation to the liver of most other animals as the much-divided kidney of the porpoise bears to the compact and solid character which this gland presents in the greater number of the mammalia.

In some animals, although the lobules are not invested by a distinct capsule, the mapping out is much more uniform and distinct than it is in others. In the liver of the rabbit, and in that of many rodent

animals, as well as in the horse, and some others, the divisions between each little lobule are more distinctly seen than in the human subject, sheep, or ox. Just as we meet with examples of the kidney intermediate between the much-divided organ of the porpoise and the solid kidney of man and many mammalia occurring in the ox, seal, and even the human fœtus, so we find that in different animals the liver presents corresponding modifications with reference to its division into lobules.

Anatomists have been too anxious to bring all vertebrate livers into the same category as that of the pig, whereas in fact the arrangement of the lobules in the liver of that particular animal is quite exceptional and peculiar. We ought rather to look upon the complete isolation of these small ovoid or many-sided lobules in this animal as exceptional than to regard it as the arrangement which exists in vertebrate animals generally. It has been found that the lobules of the human liver, and of most other animals, are in many respects very different in their form and disposition from those of the pig.

In all vertebrate animals, the arrangement in each lobule is such that the blood, after it has left the smallest branches of the portal vein, is made to traverse an extensive system of capillary vessels, from which it is again collected by the small radicles of the hepatic vein. The vessels ramifying in the portal canals seem to alternate with branches of the hepatic vein, as is shown in Pl. I, which represents the arrangement in the human liver.

In all cases, the blood, enriched by the absorption of nutrient material from the intestines, is brought by the numerous small branches of the portal vein to the circumference of the lobules, and is then made to traverse the network of capillaries, the branches of which converge towards the central, or *intralobular*, branch of the hepatic vein, Pl. II, Fig. 7. The small efferent vein unites with other branches to form at length the large hepatic vein, by which the blood is poured into the inferior cava. The blood brought by the artery pursues a course in the same direction, but the bile flows from the central part towards the circumference of the lobule. The bile and the blood from which this bile is secreted flow in opposite directions. The bile which is formed is carried away by branches of the duct. These unite to form larger branches, which run close to those of the portal vein and hepatic artery. The distension in a moderate degree of the capillaries with blood would tend to force the bile towards the ducts, but if the bile accumulated in the smaller ducts to an unusual extent, or if it became so viscid that it would not readily flow through them, or if the escape of bile from the large duct were interfered with, the free circulation of the blood through the capillaries of the lobule would not be stopped or much retarded.

INTIMATE STRUCTURE OF THE LOBULE OF THE LIVER.

We have now to consider more in detail the character and arrangement of the several structures which constitute the lobule, as may be demonstrated with the aid of powers magnifying from ten to two hundred diameters.

The lobule or elementary liver consists of a solid network of capillary vessels, in the meshes of which are situated the liver-cells. The precise relation of the cells to the capillaries is disputed, some maintaining that they are in actual contact with the capillary walls, while others consider that the cells are contained within a membranous tube of excessive tenuity by which they are separated from the capillary wall. This latter view is the one which I shall endeavour to show is correct, and, further, that in some parts of the lobule, in certain instances, not only is a membranous tube containing the cells, but between this and the outside of the capillary wall there is a space which is occupied by lymph or plasma, and which varies considerably in extent under different circumstances. In this space, in inflammation, leucocytes grow and multiply, and here a low form of connective tissue is sometimes formed which is held to play a highly important part in some of the most important pathological changes of which the liver is the seat.

The smaller branches of the portal vein which lie in fissures between the lobules and give off branches on all sides never anastomose, as some authors have described, but communicate with each other only through the intervention of capillary vessels. The capillaries of one lobule communicate with those of adjacent lobules; so that, when the marginal capillaries of several lobules are only partially injected, we observe a number of "rings" consisting of a narrow area of injected capillaries, not of single veins as shown in some works, enclosing clear spaces into the capillaries of which the injection had not extended.

The disposition of the intralobular hepatic vein appears at first sight somewhat similar. Although it may be said generally that a small branch of the vein commences in the central part of each lobule and receives capillaries which converge towards it, and which open into it direct upon all sides, the capillaries which belong, as it were, to one branch, communicate here and there with those of adjacent branches, so that in an injected preparation an appearance not altogether unlike that in which the portal vein is injected is produced. It would be difficult in looking cursorily at preparations to say in which the portal vein and in which the hepatic vein had been injected. In each case, spaces seem

to be imperfectly mapped out by the disposition of the injected vessels. Upon more minute examination, however, the difference will be easily made out, and it will be observed, first, that where the hepatic vein has been injected, the small trunk in the central part of the lobule in many instances has been cut across and remains open, because the capillaries are continuous with the vessel on all sides. The divided vein is shown by a clear and almost circular opening, in consequence of the injection having escaped in preparing the specimen. Secondly, fissures may be observed in the uninjected portions, some of them of considerable extent. Thirdly, where the portal vein is injected, these fissures are bounded on either side by injected capillaries, and contain a small branch of the portal vein which also appears clear from the escape of injection. The two points upon which we may depend for ascertaining which is the centre and which the circumference of the lobule are—the circular opening of the divided hepatic vein which is always in the centre and the fissures in which lie branches of the portal vein, hepatic artery and duct, and which are situated in the intervals between the lobules. To see these points distinctly it is better to make a very thin section, wash it carefully, place it on a glass slide, and hold it up to the light. The question cannot always be determined by examining the liver in the ordinary manner. Since it has been shown to be so difficult to distinguish between the centre and circumference of the lobules in an injected preparation, it is not surprising that without great care mistakes should arise in examining uninjected specimens; and not unfrequently the centre has been described as the circumference of the lobule, and the circumference as the centre, and mistakes have occurred in the use of the terms *portal* and *hepatic venous congestion.*

From the intimate communication between the several small branches of the portal vein through the intervention of capillary vessels, it is possible that blood passing along a small branch of portal vein should reach the lobule and travel by a circuitous route through the portal capillaries of several lobules, before it is carried off by the hepatic vein; but when we consider that blood is poured into the capillaries upon all points of the circumference of the lobules it will be observed that this arrangement would necessarily tend to cause a flow towards the centre of each lobule, and the blood would thus be carried off in the most direct manner. Supposing, however, obstruction to occur in certain branches of the vein distributed to the lobules; by reason of the arrangement above referred to the capillaries of these lobules would still be supplied with blood, the functions of the secreting structure would still be discharged, and disorganization of the lobule effectually provided against.

Of the Capillaries of the Lobule.—The walls of the capillary vessels

of the lobules are excessively thin—so very thin that were it not for the support afforded by the hepatic cells they would not be able to sustain the increase of pressure which must often result in cases in which there is some impediment to the onward flow of the blood. The walls of the capillaries are distinct from other hepatic tissues, and these vessels are developed as tubes with walls of their own, but as time goes on no doubt the wall of the capillary adheres and becomes incorporated with adjacent structures at the points where they are in contact. In the thin walls of capillaries oval nuclei can be demonstrated at intervals. In Pl. XIV, p. 112, Fig. 46, a portion of the capillary network of the lobule is well seen, with the cell-containing network occupying some of the meshes. In Pl. XX, p. 115, Fig. 68, another specimen close to the intralobular vein is represented; and in Pl. XXII, Fig. 75, a portion of the capillary network much dilated has been completely isolated.

Unlike capillary systems in other parts and organs, the capillary system of the liver is successively traversed by the same portion of blood which goes through capillary after capillary until it is poured into the large intralobular venous branch. Many deleterious substances absorbed from the intestinal surface, and carried to the liver by the portal vein, would thus be slowly changed so as to be rendered innocuous before the trunk of the hepatic vein was reached. This extensive so-called solid capillary network of the lobule of the liver with its fifty or more continuous meshes and necessarily slow blood current constitutes an arrangement very favourable for the growth and multiplication of bacteria, and for the disintegration and chemical decomposition of substances in the blood whereby the system may be infected.

The liver stands as a sentinel which guards the points of entrance of all materials taken up from the intestinal surface for the general circulation. It seems to me very likely that in this way also noxious matters, such as virulent bacteroid bodies and organic matters in a state of chemical change, may be taken up from the surface of ulcers in some part of the alimentary canal. Things in the intestines having damaging properties may be transformed and changed to the great advantage of the patient whose liver is in a normal healthy condition, while, on the other hand, if this important organ is not in a healthy state, by the passage of such noxious matters into the circulation, serious disease and death might quickly follow. In this way perhaps may be explained the recovery after very severe attacks of typhoid fever, cholera, yellow fever, and dysentery, and the fatal result in forms of the same diseases much less severe. A healthy state of the minute structure of the liver, and healthy lungs of good capacity, greatly increases the prospect of recovery from many forms of serious disease. If we would form an estimate of the probable course and result of any given case of serious illness, due weight must be given to these important considerations.

When we consider the very extended course of the capillaries of the lobule we shall not feel surprised that disturbances in the circulation often determine grave modifications in the action of the secreting cells, which may soon occasion alterations in the blood and derange the action of the most important tissues and organs in the body, or lead to permanent and irremediable structural changes. It is obvious that congestion of the capillaries and slowing of the uniform slow circulation of the blood may operate in retarding or altogether stopping for a time the secreting action of the cells by the pressure exerted upon all sides. Such pressure having been exercised for some time leads to other changes. Not only must the cells suffer as regards their nutrition, growth, multiplication, and action, but, the blood not being properly depurated by the removal of the substances it is the office of the liver-cell to take up, acts deleteriously in all parts of the organism, and causes in many cases great pathological disturbance resulting in a serious and very likely prolonged attack of illness.

Arrangement of the Cells.—At the circumferential part of the lobule the cells are arranged so as to exhibit indications of an irregular network, but towards the central part the cells are more linearly arranged, and in many livers it is difficult to believe they are not actually in tubes so arranged as to form a network with elongated meshes. Either as columns of cells or tubes containing cells there is a convergence from the circumference to the centre of the lobule. It has long been a question whether the cells are disposed in the meshes of the capillary network or whether they are enclosed in tubes of delicate membrane. The cells are prone to become detached in the form of little columns which are often branched, an appearance which is usually considered to be due to the manner in which they are fitted into the vascular meshes, and not to the presence of any tissue surrounding them, which would keep them together in this manner. In these detached masses indications of tubular membrane may be often seen, but it is seldom in the specimens so prepared that any distinct evidence of a tubular membrane can be obtained. The apparent connection of the cells with one another has been accounted for by a supposed adhesion of the cells.

Question of the Existence of a Tubular Membrane in any part of the Lobule of the Liver, and within which the Cells lie.—Among the authorities who have advocated the existence of a cell-containing tubular membrane may be mentioned Krukenberg, Schröder, Van der Kolk, Retzius, Weber, Theile, Backer, and Leidy, while Kiernan more than fifty years ago described a *lobular* biliary plexus, the tubes of which were considered by him to be continuous with the ducts. More recent observers have arrived at a very different conclusion, and during the last twenty years or more the existence of such a membrane has been

denied, and it is now taught that the bile formed upon the surface and in interior of the elementary part is received by excessively fine ducts.

It is not uncommon to find cells with delicate membranous shreds attached to them in specimens which have been slightly hardened in dilute alcohol. In some cases cells are found enclosed in a membrane which can be traced in the interval between them as a very narrow contracted tube. From time to time, upon carefully examining the edge of a thin section of liver mounted in glycerine or syrup, small portions of the network are seen to project, but it is not possible to demonstrate the existence of such a membrane when the preparation is examined in water or spirit. In sections which have been mounted in glycerine a distinct tubular membrane can often be seen. I have observed the same point in several preparations, but have been unable to preserve the specimens permanently. The extreme thinness and delicate nature of this membrane will readily account for the difficulty of displaying it, and it must be borne in mind that, in the majority of specimens examined in the ordinary manner, it is impossible to see even the walls of the capillaries, which are so much thicker and firmer than the cell-containing tubular membrane. The difficulty of demonstrating such a membrane seems to me but a very insufficient argument against its existence ; and, even if it were quite impossible to see it, it would hardly be right to conclude that it was absent upon these grounds. It is possible for such a membrane to exist, and to be at the same time quite invisible, unless rendered more or less opaque by some peculiar mode of preparation.

Fusion of the Contents of the Membrane.—This delicate basement membrane is well displayed in certain specimens in which a curious chemical change has taken place in the contents of the tube. In a section of dog's liver which had been soaking for some time in a weak solution of soda the outer portion of most of the cells appeared to have been dissolved, and, in consequence, a fusion of their substance had taken place, causing the formation of a highly refracting mass within the basement membrane, the outline of which was rendered very distinct.

A somewhat similar change has been observed in the liver of a flounder which had been treated with soda, and afterwards by acetic acid, which caused the precipitation of some of the constituents of the bile which had been previously dissolved by the soda. By pressure some of these highly refractive masses were broken, and by examination with a very dull light the continuity of the delicate basement membrane could be traced between them. When certain specimens of liver have been soaked for some time in strong syrup or glycerine, the cells in the interior of the tubes shrink from exosmose, and the delicate tubular membrane contracts upon its contents. The tubes, therefore, become

much narrower, and, excepting in the highly refracting nature of their contents, the altered cell-containing network closely resembles the capillary network.

Capillaries displayed in one section, and Tubular Network in another section, from the same Liver.—In a properly prepared liver it is often possible to demonstrate the cell-containing network in one section, and the capillary network in another (Pls. XIV, XX, XXIII, Figs. 46, 68, 79). When the vessels are distended with clear size, the meshes of the cell-containing network are seen; but, if a section be well washed and placed in glycerine, the sharp well-defined outlines of the capillary vessels are brought into view. In such a section, from which the cells have been removed, I have seen in some places, just at the thin edge of the specimen, stretched across the space between two capillary vessels, the exceedingly delicate basement membrane of the tube in which the liver-cells lie, recognizable rather from the small quantity of *débris* and granular matter which adheres to it than from any positive characters distinguishable in the membrane itself. This appearance can only be seen under the influence of a very dull light. I have one preparation preserved, in which the membrane is demonstrated very satisfactorily, for the delicate tube projects beyond the cells for a short distance.

Distension of the Tubes by Injection.—The network is capable of being distended to a considerable extent in every part of the lobule without rupture. Often the injection accumulates to such an extent as to completely obscure the cells; and, in consequence of the pressure thus caused, the capillaries may be so compressed as to be rendered invisible. Even in such specimens, the appearance cannot be mistaken for extravasation from vascular injection. In tubes which are only partially injected, the injection often accumulates more in one place than another, and sometimes it collects a little on each side of the tube around the cells, gradually shading off, as it were, towards the centre; while towards the adjacent capillary vessel it forms a well-defined line.

A portion of the cell-containing network, and its junction with some of the finest ducts, from the human subject, injected with Prussian blue, is delineated in Pls. XII and XIII. In the pig, portions of the cell-containing network in different states are represented in several figures in Pls. XVI, XIX, and XX. The arrangement in different parts of the lobule in the pig's liver is very distinct, Pls. XIX and XX. But the question of the connection between the ducts and cell-containing network will be fully considered in a special section. *See* page 100, *et seq.*

Radiation of the Tubes from the centre of the Lobule.—If in certain instances a section be made through the lobule, exactly at right angles to a small branch of the intralobular vein, the cells are seen to be arranged in rows, which radiate from the centre towards the circumference of the lobule, as has been noticed by Müller, Valentin, Bow-

man, Theile, Gerlach, and others. In sections made in other directions, this radiated arrangement is not to be shown. In the horse's liver is to be seen a beautiful specimen of this arrangement. The rows increase in number as they pass from the centre. They are connected at irregular intervals by oblique or transverse branches, often much narrower than a full-sized cell, and which contain only nuclei and granular matter. These communicating branches are best seen in injected specimens. The cells of which the rows are composed for the most part form single lines, although here and there, where the tubes are wider than usual, two cells may be seen lying transversely across the tube. A well-prepared specimen of this kind appears to me to prove the existence of the tubular network in the lobules of the liver almost as distinctly as a good preparation of the kidney demonstrates the presence of long tortuous tubes in the cortical portion of that organ.

In specimens in which these radiating tubes have been injected, not only has the existence of a basement membrane been proved, but one distinct from, and not adhering to, the walls of the capillary vessels. The meshes of the capillary network are slightly elongated towards the centre of the lobule, but it is obvious that such an arrangement could not alone account for the appearance observed; for if the cells lay promiscuously in the meshes of the capillaries, without being circumscribed by any tubular membrane, the radiating lines would necessarily be connected transversely by numerous cells, forming a wide stratum. They, however, are only united by narrow tubes containing a single row of small cells or granules.

In an injected preparation of the rabbit's liver which was carefully removed from the upper surface, the tubular arrangement was very distinctly demonstrated. The specimen is represented in Fig. 44, Pl. XIV, p. 112.

Diameter of the Tubes of the Network.—The contents of the cell-containing network are liable to considerable alteration in volume, a change which can be readily effected artificially. In the same specimen the diameter of the network varies, but only to a very limited extent, according to the size and number of the cells within the basement membrane. It is usually about 1-1000th of an inch in diameter in most mammalian animals, and is considerably wider than the narrowest part of the ducts with which it is immediately continuous.

The width of the spaces between the tubes of the network, or, in other words, the diameter of the vessels, varies much in different parts of the lobule of the human liver, being much wider at the portal surface of the lobule, where the small branches of the veins enter, than at a greater depth, where capillaries are alone found. This point is well seen in a thin section from the lobule of the liver of the fœtus.

Interval between the Walls of the Capillaries and the Membrane of the

Tubular Network.—In the fœtus a distinct interval between the wall of the tube in which the secreting cells lie and that of the capillary vessels can be clearly demonstrated, so that, when a good section is obtained, two distinct lines are seen between the hepatic cells and the cavity of the capillaries, Pl. XX, Fig. 68. These two lines are separated by a perfectly transparent, apparently structureless material, probably fluid or semifluid and varying in quantity, in which no trace of fibres can be detected. Here too are situated the finest ramifications of the nerve-fibres which pass into the liver upon the walls of the portal vein, hepatic artery, and ducts, and form wide and extensive networks of excessively fine fibres, with numerous oval nuclei at intervals very close to the capillary walls.

The capillary network and the cell-containing network do not exactly correspond.—And lastly, there is the fact already alluded to, that the capillary network does not exactly occupy the meshes formed by the arrangement of the cells, while it may be made to do so if very fully distended with injection as in Fig. 75, Pl. XXII; *see* also Fig. 79, Pl. XXIII. In certain chronic morbid changes in which gradual contraction of the cells has been going on for a considerable time, the tubular membrane in which the cells lie may be seen clearly enough in consequence of some thickening having taken place, Fig. 75, Pl. XXII, p. 184, near the central part of the lobule; in such a case both the capillary network and the cell-containing network exhibit elongated meshes. This renders it certain that the two sets of tubes are not complementary and mutually fitted into one another. Narrow transverse intercommunicating branches of the cell-containing network can be demonstrated without difficulty. It therefore appears to me certain that the cell-containing network in which the liver-cells lie is a tubular structure altogether distinct from the capillary walls, though it is probable that at the points where the two networks are in contact the membranes may become connected together.

The two vascular and cell-containing networks grow *pari passu*, and I think it probable that during development diverticula or cæcal prolongations are formed here and there, and project into the new meshes, being formed in connection with the capillary vessels, as in the vasa aberrantia, and as represented in Figs. 52 to 56, Pls. XVII and XVIII, from the liver of the toad. One can imagine a tube with numerous diverticula as represented in Pl. XVII becoming much more complicated by the extension and subdivision of the diverticula.

In connection with this matter I think the reader should carefully study the figures in Pls. XVII, XVIII, p. 114, because they will enable him to form a correct idea not only of the actual arrangement but also of the manner in which a highly complex reticulated arrangement, as seen in the whole of the vertebrate liver, at length

results from the extension and subdivision of very simple tubular beginnings.

The circumstances above enumerated impress me with the idea that the liver is originally composed of two distinct networks, which inter-digitate with, or fit into, each other—one containing the secreting cells, —the other the blood. As development proceeds, the walls of these two sets of tubes gradually come into contact, and are perhaps incorporated here and there. In those situations where the capillary network is less dense, or where the meshes of the cell-containing network are more widely separated from one another, a distinct limitary membrane to the tubes containing the liver-cells can be demonstrated in the adult. The cell-containing network and the vascular network can be alternately distended. The membrane of both is very permeable to *water* in both directions, as I have proved by first forcing fluid from the vessels into the duct, and afterwards in the opposite direction. Subsequent injection proved that no rupture had taken place. Nevertheless, the greatest force which can be applied will be found insufficient to cause the bile to pass through this delicate membrane into the capillary vessels.

Under some circumstances, then, it is demonstrable that the basement membrane of the cell-containing network is distinct from the walls of the capillaries; but in the greater part of the lobule, where the two membranes come into contact, the majority of the liver-cells, except at the points where they are in contact with each other, are surrounded with blood, from which they are only separated by a thin layer of delicate structureless membrane. Bile formed at any part of the network would find its way between the cells and the tube of membrane to the margin of the lobule. Upon the other conclusion, which supposes that the cells lie freely in the meshes of the capillary network, the bile formed in the more central part of the lobule is supposed to be transmitted from cell to cell, until at last it reaches those at the circumference of the lobule, or, that it is taken up by the supposed capillary gall ducts, some of which impinge upon the cells. If bile were formed by being passed on from cell to cell in the manner that has been suggested by some, the materials from which the crude bile is first formed ought to be separated from the blood in the more central parts of the lobule; for, otherwise, the blood, rich with recently absorbed constituents, would seem to pass through a considerable extent of that portion of the capillary network at the circumference of the lobule to no purpose. If the arrangement of capillary gall ducts is correct, it ought to be shown why the cells in the more central parts of the lobule are as fully supplied as those at the circumference, it being quite certain that the greatest activity of bile formation occurs at the circumference of the lobule.

If then the description I have given of the anatomy of the parts be correct, the precise point of the most active formation of bile should be

the outer part of the lobule, for the blood reaches this part first. It will be shown subsequently that this is really the case. Argument alone would render the existence of a membrane probable, but, with care as has been stated, its presence may be actually demonstrated, and by several different methods of preparation.

CONTENTS OF THE TUBULAR NETWORK.

The highly important anatomical elements contained in the tubular network of basement membrane are the *liver-cells ;* but, besides these, a small quantity of free granular matter is always present, and not unfrequently oil-globules and granules of dark yellow colouring matter are met with. In disease, it is not unusual to find the network occupied by a viscid, granular, highly refractive mass, in which here and there only a few nuclei can be observed. Sometimes the cell-containing network is so shrunken as not to be more than half the diameter of an ordinary healthy hepatic cell, and its contents appear to consist of a viscid material, in which are suspended granules and oil-globules. In fishes generally, the tubular network seems to be greatly distended, and entirely occupied by a mass of oil-globules. With care, however, new centres, nuclei, may sometimes be distinguished among them. These can be rendered perfectly distinct if they are properly stained with carmine fluid.

In the class of fishes, and in some reptiles and birds, and, according to Dr. Handfield Jones, even in the rat, the tubes of the cell-containing network do present the appearance of being filled with an uninterrupted mass, composed of oil-globules, granular matter, nuclei, and sometimes coloured granules. In the cell-containing network of the common eel (*Anguilla acutirostris*), this point is well shown. The tubes are seen filled, but not distended, with oil-globules. The highly refractive power of the latter prevents the possibility of the nuclei being seen *in situ ;* but at the edges of the section and in the fluid surrounding the preparation a few were distinctly observed. In such a preparation the disposition of the contents of the tubular network in fishes is well shown ; and it demonstrates, in an uninjected preparation, the existence of the tubular membrane, so difficult to show in this class of animals. In another part of the same liver the capillaries were injected, and their arrangement is very similar to that in most animals. In the eel's liver the tubes containing the oil-globules form a lax network with very long meshes, or perhaps the specimen might be more correctly described as being composed of parallel tubes, communicating with each other here and there. Now we may enquire how such evidently cylindrical lines of oil-globules as exist in this liver can be arranged as we see them in the meshes of the vascular network, unless they lie within a tube of basement membrane? Of the

accuracy of the facts there can be no doubt, and the only explanation I can offer of the appearances observed, is that just advanced.

In a large number of animals, then, the contents of the tubular network may be said to be continuous; in some it is interrupted so as to form masses irregular in size, in which nuclei are scattered at intervals; and in others, the masses (cells) are more uniform in size, resemble each other very closely in general character, and each contains a separate nucleus. Between the numerous, well-defined, and separate masses, or liver-cells of the mammalian animal on the one hand, and the continuous mass which occupies the tubular network of the fish on the other, it is easy to obtain specimens illustrating every degree of difference. More than this, at different periods of development of the embryo, and in various morbid conditions of the human liver, every degree of separation and of continuity may be observed. Again: by the action of various chemical reagents, the distinct and separate cells of the healthy mammalian liver may be made to fuse, as it were, so as to form continuous masses, like those occupying the tubular network of fishes.

In all cases there is room for fluid to pass between the contents of the tube and its walls towards the duct, as may be proved by the passage of injection; and, although to our observation the tubes may appear to be quite full, or even distended, it is obvious that, independent of any change of size in the cells themselves, a very slight diminution in the quantity of blood in the capillaries of the liver would permit the free passage of fluid along these apparently distended tubes.

The facts I have stated tend to lead to the conclusion that the liver-cell is to be regarded as a collection of viscid matter round a central nucleus, rather than a true cell provided with a distinct cell-wall.

Of the manner in which the Cells are arranged within the Tubular Membrane.—In the livers of adult mammalia which I have examined, the cells for the most part lie in a single row, although, as before observed, some portions of the network have been found to contain two or three rows lying across the tube, while in other situations the space within the tubular membrane is so contracted as not to admit one cell of the ordinary size, in which case it is occupied only by granular matter, and a viscid material which refracts highly. The following mammalian livers have been examined with reference to this point,—that of the human subject, pig, dog, cat, rat, rabbit, horse, seal, and some more.

I have never seen such an appearance as has been delineated by Leidy, who has represented three cells lying across the tube; nor have I observed anything agreeing with the description or drawings of Lereboullet, who figures two rows of cells, and represents a mass of injection passing between them. My own observations lead me to conclude that the cells lie somewhat irregularly, as above described, and

differ totally in their arrangement from that of the renal tubes, where there is a central cavity. Bile would escape from the cells, and pass in an irregular manner, sometimes on one side of the tube, sometimes on the other between the cell and the wall of the tube, and this is the way in which injection can be made to pass in the direction opposite to that in which the bile flows naturally.

In the only embryos of mammalia which I have examined, more than one row of cells is contained within the tube, and two or three are commonly met with (human fœtus, fœtus of ox). The cells are smaller than in the adult liver, the tubes not unfrequently being larger. In birds also (linnet, turkey, starling, fowl), two or three cells lie within the tube in some places, but in others only one is met with. In the embryo-chick numerous rows of cells are seen lying across the tube (Fig. 72, Pl. XXI).

In the livers of those reptiles which I have observed, there are often several cells lying across the tube (frog, adder, field-snake); in some fishes there is also room for many rows of cells (flounder, frog-fish, sturgeon, herring, cod, &c.).

Hering showed that in the snake's liver there was a central channel along which the secretion escaped from the cells into a central space as in the kidney. In Fig. 51, Pl. XVII, p. 114, from the frog, a similar arrangement is shown, and in parts of the liver of the toad and newt the same disposition exists.

It may be said, generally, that the tubes are most narrow amongst mammalia, and widest amongst fishes. The "cells" also are well defined in the former, but not often demonstrable in the latter class. The similarity of the arrangement of the cells in the tubes of the embryos of man and the higher animals, to that which exists in the embryonic, as well as the permanent condition in the lower vertebrata, and in many of the invertebrata, is a point of interest, and one which has a parallel in the case of some other glands and many tissues. There is perhaps no more striking example of this gradual progress from the lower and simpler form of structure to the higher and more elaborate than the one here adduced.

THE ESSENTIAL HEPATIC ELEMENT AND THE QUESTION OF ITS ACTION.

Of the Liver-cell, its Nucleus and Nucleolus.—In all animals, and from that early period of existence when the organ is first developed to the very end of life, one of the most important duties discharged by the liver is to alter and prepare certain constituents recently absorbed from the intestinal surface to fit them for introduction into the blood. Albuminous, fatty, and starchy matters, or derivatives from them, are taken up by the liver-cell, and by its agency changed. It is certain that the operation of the liver-cell is as important and as necessary to the well-being of the organism in the case of the exclusively flesh feeding creatures as to those which live on vegetable matter only. The changes to which starch and the nitrogenous class of substances are subjected in the mouth, in the stomach, and in the upper part of the alimentary canal, cannot be regarded as in any way supplementary to or taking the place of the important action effected by the liver, for the liver exists in cases where the secretions to which the food is subjected before it is brought under the influence of hepatic action are entirely absent:—nay, where no salivary glands, gastric glands, duodenal glands or follicles are to be found, and even where there is no proper mouth or stomach. In the higher vertebrata, at a period long before the organisms above referred to are called into activity, the liver-cell is active and is engaged in effecting changes of the most important and essential character in the constituents brought to it in the blood prior to their introduction into the general circulation and their application to the nutrition of the developing tissues.

It is probable that some of the organs of invertebrata hitherto considered to be of the nature of a liver really perform some function in the economy not precisely the same as that discharged by the liver of man and the higher animals. And it is not impossible that offices performed in man and mammalia by the liver, pancreas, and some of the intestinal glands, may be discharged by a special organ which anatomically at least seems to be mainly hepatic. In considering questions of this kind many observers have I think too exclusively regarded the matter from the point of view which assumes that man is in all respects the highest and most perfect type of animal, and that all other creatures are his inferiors as regards all functions. But man can be shown to be higher only in some respects than many creatures, while

as regards certain glandular organs, his muscular system, and parts even of his nervous system, these are low indeed in comparison with the corresponding tissues of many organisms usually considered far inferior to man in the scale of creation.

With regard to the manner in which the liver-cell acts upon the matter presented to it and effects its change, the greatest difference of opinion exists. Some think that a mysterious met bolic action is exerted by the nucleus, but how is not even suggested. Physiologists who have committed themselves to purely physical explanations of vital operations think nothing of assuming the existence of *properties* and *agencies* which are excluded from the physical category. Thus it is supposed the liver-cell or its nucleus or the nerve supposed to end in it changes the matter as it comes near it, altering its composition and causing the formation of new compounds, but such a suggestion is a pure speculation.

Where, as in man and the higher vertebrata, the liver attains a high degree of development, and its proper action is absolutely essential to the free and vigorous discharge of function of the most important tissues and organs, the arrangements for effecting and facilitating the thorough depuration of the blood as it flows through the capillaries of the liver are wonderfully perfect and clearly designed for carrying out this object. That the liver-cell is in a most important degree though not exclusively concerned in the preparation of matters to be used for the nutrition of the nervous and muscular systems is very probable, but at the same time it is certain that its work is not limited to this purpose; for, although there is a general relation between the size and activity of the liver and the nervous system, the agreement is not in all cases sufficiently marked to justify us in accepting this conclusion as of universal application.

The cell varies much in form and size in different animals, and in different parts of the lobule of the liver of the same animal. Its characters have been well described by numerous authors. The largest cells are not unfrequently as much as 1-800th of an inch in diameter, the smallest not more than 1-2000th of an inch, or even less.

In all the animals which have fallen under my notice, the liver cells, compared with the cells of other glands, are remarkable for their variety of form and size, for their high refractive power, and for containing, besides the nucleus, granular matter, and, very frequently, oil-globules and granules of yellow colouring matter. Under some circumstances the yellow colouring matter becomes much altered, and so dark, that the cell appears to be occupied by black granules, which are sometimes very numerous. Sometimes minute crystals of a dark green colour (biliverdin) are present in the matter of which the body of the cell is composed. The material of which the cell consists is not of a fluid

nature, but highly viscid; so that, upon pressure, the whole cell becomes flattened, and the highly refractive viscid material is seen to form a thin layer.

Some cells are rounded, others oval or polyhedral in form, and certain exceptional cells present many irregular angles, with somewhat rounded edges. Not unfrequently the appearance is such as would give one the idea that the cells had been packed together very closely, and thus subjected to pressure unequally distributed. The *cells* in some cases look like fragments broken off from a solid, more or less cylindrical mass, originally continuous, in which nuclei had grown here and there—a view which accords in some degree with one formerly held by E. H. Weber.

Each cell contains a nucleus, easily demonstrated in perfectly normal cells; but not to be readily distinguished when the cells contain much oil, and when they have undergone other changes in the course of disease. The nuclei vary considerably in size. Upon an average, they may be said to be about the 1-3000th of an inch in diameter. Generally they are circular, but sometimes they have an oval form. The nucleus contains granules, some being larger than others; often there is a bright point in the central part, which is regarded as the nucleolus, but is in many cases only an oil-globule. Each liver-cell of the adult liver usually contains but one nucleus; but, in some instances, two or more may be observed. The liver-cells of young animals commonly contain many nuclei. I have observed as many as six or seven in the cells of the calf, about the middle period of gestation.

The so-called nucleus varies greatly in size according to the rapidity with which the cell changes proceed. If nutrition is active not only will the nucleus increase in size, but it may divide, and if the conditions favourable to the nutritive process persist for a considerable time the nucleus may grow and subdivide into several nuclei. In each of the bodies resulting from subdivision, a nucleolus or new centre may appear, and sometimes more than one may be discerned. It must, however, be borne in mind that the term nucleolus has often been applied to an oil-globule which has nothing whatever to do with the action or nutrition of the cell. In no case ought the term nucleolus to be applied to an oil-globule.

The "liver-cell" was not known when Kiernan wrote in 1833, and it was not until after the researches of Schwann and Schleiden that observers began to recognise in this small body the necessary active agent by which the remarkable disintegrative alterations in certain chemical compounds presented to it were brought about, and the recombination of the elements into compounds of very remarkable chemical composition and properties effected.

Even now our knowledge concerning the action of the liver-cell, or

elementary part, is imperfect, and inexact in many particulars, and no one, after the most careful study of its structure and composition, has been able to explain by what means it formed bile, altered albumen, and caused the appearance of a substance not far removed from certain forms of sugar; and so re-arranged elements of the compounds it acted upon, as to produce such highly complex and peculiar bodies as glycocholates and taurocholates. Some essay to have solved this and other questions by affirming that the wonderful metabolic actions are certainly due to the "properties" of the chemical constituents of the matter of the cell, but such affirmations are as preposterous as they are unscientific, and only indicate an attempt on the part of those who make them, to impose upon simple folk, to stifle reason, and stop investigation.

It is certain that the thin membranous vesicle, or cell-wall, closed at all points, which has for many years been regarded as an essential constituent of the cell, and is even so described by some to this day, does not exist in most cells, and where it is present it is not of any physiological consequence. Neither in cell origin or growth, cell action or multiplication, does a cell-wall play a necessary part,—while all these phenomena proceed in elementary parts, altogether destitute of cell-wall and indeed of cell-contents, as these are usually described.

A defined outline as seen in objects under microscopical observation is often misleading, for it has been too often inferred that this line indicates a limitary membrane. A thin layer upon the external surface of many a mass of bioplasm no doubt consists of matter in a very different state from that which constitutes the mass, and sometimes this is condensed so as to form a thin membrane or film, which deserves the name of a cell-wall; but neither this, nor the smooth delicate transparent layer of excessive tenuity, not unfrequently to be demonstrated, is necessary to the cell or its action. As is well known, in many cases, there is no limitary film or membrane of any kind, and yet the "cell" lives, and grows, and acts, and forms, and multiplies. The persistent idea of cell-membrane has dominated men's minds, and has interfered with, and still interferes with, the acceptance of reasonable views concerning life and action.

In like manner the nucleus, as we see it, is often bounded by a sharp line, and this has been supposed to indicate a cell-wall, by which the matter of the nucleus is supposed to be separated from the matter around it. The appearance of this dark clearly defined line is in many cases optical only, and results from a difference in the refractive power of the matter of the nucleus and that of the cell. Moreover, the difference in question is much greater in some cases than in others, while it varies from time to time in the very same cell, according to the rate at which nucleus growth takes place. But whether the line forming

the circumferential limit of the nucleus appear to be thick or thin, indistinct, or sharply cut and well defined, it is not due to any limitary membrane. The matter of the nucleus is not in a closed bag which can shrink or be stretched according to the varying quantity of its contents, and in life the size of the nucleus does vary considerably, but it consists of living matter which has grown from a pre-existing speck of living matter in the substance of a mass of bioplasm, which had existed and had grown for some time before any indications of a new centre of growth were present. And if the nucleus we are observing had remained in the living body for some time longer, a new centre or more than one would have made its appearance. The cause of the origin of these new centres is intimately connected with the consideration of the nature of life itself, and cannot be pursued here.

But so firm is the conviction that some "structure" exists in the cell and in the nucleus, which if it could be demonstrated would certainly enable us to explain, or would lead us towards the explanation of cell action, that generation after generation goes on structure hunting, and some of the most distinguished among observers appear to be so infatuated with the idea, that their broad general conclusions concerning life and action seem to be chiefly based upon the view that structure everywhere exists, and by its variation varying function is determined. So memoir after memoir is devoted to the minute description of granules, lines, membranes and the like, which have been demonstrated in the cell or in its nucleus. But no one has shown how such bodies account for the changes effected. Nor has any one even ventured to suggest in the roughest way the sort of apparatus, or machinery, or structure, that would be effective in producing compounds having the characters and properties of those of which the secretion is composed. Nor can I understand how the tissues, or tissue spaces, the threads, the lines, fibrils, reticulations, reticulated appearances, granules, and other things that have been seen bring us in the slightest degree nearer to an explanation of the mode of production of the secretion. We might admit the presence of any and all the structures that have been described, and many more that have not been seen or supposed to exist, and we should still be just as ignorant concerning the production of glycocholic or taurocholic acid as we are now.

But before the question of the action of the liver-cell and the nature of the secreting process can be profitably debated, it will be necessary to consider the arrangement of the finest ramifications of the nerve-fibres in the liver, and the probable action of these and the nerve-cells on the hepatic secreting cells. This gland is exceptionally favourable for the enquiry, on account of the very large amount of secreting structure it contains free from other texture, and the abundance of the secretion formed by the cells. If nerves act directly on secreting

cells, it is in such an organ we should look for positive evidence of the fact.

OF THE FINEST NERVE-FIBRES IN THE LIVER; THEIR RELATION TO THE CELLS AND OF THEIR ACTION.

I have seen very fine nerve-fibres forming an extensive network around the tubes containing liver-cells in the newt, frog, and toad, but the peritubular plexus of very fine nerve-fibres is less extensive than that found about the uriniferous tubes of the same animals, Pl. V, Fig. 15, p. 48.

The fine nerve-fibres do not belong exclusively to the capillary vessels, but ramify on the external surface of the cell-containing tubules, which they touch here and there, and then run perhaps for two or three thousandths of an inch without coming into contact with the walls. These fibres are less than the one hundred-thousandth of an inch in diameter.

The finest nerve-fibres distributed to the liver, like those in other tissues, are connected with oval masses of bioplasm which, however, are not larger or more numerous than the corresponding nuclei found in connection with fine nerve-fibres distributed to some of the lower and passive tissues, as, for example, fibrous tissue. Indeed the nuclei are very much less numerous, and are separated from one another by considerably greater intervals than in the case of nerve-fibres distributed to mucous membranes, to the skin, and to sensitive surfaces and tissues in general, or to muscular fibre both striated and non-striated.

Looking from the anatomical side, the small number and size of the nerve-trunks, the sparing distribution of the fine nerve-fibres in the substance of the liver, and the small size and number of the nuclei, would certainly lead us to infer that the liver was not one of those organs the action of which mainly depended upon the nervous system. To all tissues and organs containing blood-vessels nerves are distributed, but the nerve supply of the vessels of the liver is small as compared with that of some other glands; and in this particular the liver does not widely differ from ordinary fibrous tissue. It is therefore most improbable that the most important functions of the organ are dependent for their proper discharge upon the nervous system.

In no case have I been able to satisfy myself that any nerve-fibres formed a plexus on the external surface, or came into contact with or actually entered epithelial cells. Nor have I ever met with appearances which would justify the inference that the finest ramifications of nerve-fibres terminated in or were in any way connected with the liver-cells or their nuclei. Both in the liver and in the kidney of several batrachia I have searched in vain for such appearances, and in every way that

seemed to afford any chance of success. While I was able to demonstrate the arrangement of many very fine nerve-fibres not previously figured, I could never see any indications of the appearances represented in the drawings of fibres much coarser than those I had demonstrated, by observers who declare that they have established the fact of a structural connection between nerve-fibres and secreting and other cells. As regards the question of the passage of the axis cylinder of the nerve-fibre into the cells, I feel sure that this is not the case in the liver-cell. I say "sure" because I have traced far finer nerve-fibres *around* the tubes and about the cells than those who maintain the entrance of the axis cylinder have figured in their drawings, and I have followed the ramifications of very fine nerve-fibres less than the one hundred thousandth of an inch in diameter, for long distances. If the supposed ultimate connection or actual blending of structure between secreting cell and nerve-fibre were a fundamental arrangement and necessary to the process of secretion or to its proper regulation, one would expect to find the bundles of nerve-fibres distributed to an organ varying in size according to the number of the cells. In the case of the liver, which contains many times the number of cells present in any other organ in the body, the nerve-trunks are even smaller and the fibres far less numerous than we should expect to find if the arrangement above referred to existed in nature.

It is remarkable that of those who profess to have traced nerve-fibres into secretive epithelial cells, many depict the connection as being situated not far from that part of the nerve-fibre where the medullary sheath or white substance of Schwann exists. Now from my own observations I am certain that very fine fibres run many hundredths of an inch beyond this point where the medullary sheath ceases, without entering or becoming connected with a secreting cell or any other structure; while in so many cases I have demonstrated the disposition of these fine fibres as a lax network, that I cannot but accept the view that this is the general arrangement and expresses the general relation between nerves and the tissues they influence.

Undoubtedly the ultimate arrangement of nerve-fibres in all tissues and organs can be proved by observation only, but at the same time it is right to urge that in the absence of positive demonstration opinions should be expressed with caution and doubt. Instead of this, so many erroneous statements and drawings have been made, and with great confidence, and have been received as if they were true, that it is most difficult for any one who has not actually worked at specimens to approach the question with any prospect of ascertaining the truth. As far as I am able to judge there is no justification for concluding either that the secreting process is determined by nerve action or that nerve centres act directly upon the secreting cell, or that the latter cannot

produce its proper characteristic secretion without the direct influence of the nerves and nerve centres. The fact of the formation of highly complex chemical compounds in the plant cell alone goes far to prove that the secretory process is not essentially dependent upon nerve action. While nothing that is known of the actual changes occurring in bioplasm or the formed matter resulting from it suggests that the changes in question in any way depend upon nerve-currents, while the fact of the formation of substances of a highly complex chemical composition, at a period of embryonic development antecedent to the formation and action of nerves and nerve centres, is suggestive of a very different conclusion. In short, there is no more reason for the assertion that the production of biliary matters is due to any nerve influence than that the formation of starch or sugar gum is dependent upon nervous action. Whatever part the nerve-fibres may play in the processes going on in the liver, the evidence in favour of the general secretory processes being intimately connected with nerve action is most inconclusive, and, if the judgment is to be influenced by demonstrated facts, the conclusion would be that no mere formative or forming process in nature can be regarded as due to nervous action or solely to nerve influence.

It is, I think, to the investigation of the exact influence exercised by parts of the nervous system upon the secerning process that attention ought to be directed. The view that the action of nerve organs on secerning cells is direct is mere assumption, while concerning the mode in which the assumed direct action is exerted, there are no facts upon which reasonable hypothesis can be framed. So far nothing but pure speculation can be advanced. And surely it is premature to speculate as to the manner in which the nerve-current may affect the process of secretion as it proceeds in the cell, while the real nature of the nerve-current itself remains doubtful. It will surely be very unprofitable to look for an explanation of the secreting process in nerve influence, while we do not even know what changes occur in the ultimate parts of any sense organ when an impression is produced, or the difference between the same nerve organ when it is actively engaged in receiving impressions and when perfectly passive. But, if we admit the probability of the supposition that the secretory process is due to nerve action, we must bear in mind that no one has yet offered any reasonable suggestion as to the exact way in which the nerve-current may determine or modify the metabolic phenomena undoubtedly taking place in the cell. In short, the theory takes us no nearer to the process of cell change than we were before the help of nerve-agency was invoked, and then authoritatively affirmed.

OF THE NATURE OF THE CHANGES EFFECTED BY THE LIVER-CELL IN HEALTH.

If then we are obliged to acknowledge that the facts of the case almost compel us to give up our belief in the doctrine advanced some years ago and still current, that in some way or other not yet ascertained nerve-action is the direct cause of the formation of those marvellous and highly complex chemical compounds which appear in the countless infinitesimal laboratories with which the whole of living nature teems, we almost feel forced to attempt some other solution of the difficulty, and we try to frame some hypothesis more in accordance with well-known facts. The formative processes going on under our very eyes, though invisible to us, and in every part of our own organisms, must have an explanation, and every real student longs to learn how far the knowledge we have tends to lead us towards a solution of this most important problem.

That the special substances constituting the secretion of a gland are formed from and by the bioplasm or living matter of the cell may be considered certain. This living matter has been called protoplasm, but that name has unfortunately been applied to matter which is not living, as well as to the matter of the cell actually alive. It is the living matter only which possesses the power of chemically disintegrating the matter which constitutes the pabulum of the cell and of effecting constructive chemical changes.

The material to be changed by the liver-cell must be presented to it in solution, and the course taken by this solution may be proved by placing a little alkaline solution of colouring matter close to the cell of the liver of a recently killed animal very soon—half a minute—after it has been removed from the body. In the course of a few seconds an ammoniacal solution of carmine will traverse the outer part of the cell and reach the nucleus, which becomes stained red. In life certain substances in the solution which transudes from the blood are taken up and appropriated by the living matter of the cell. The matter formed by the nucleus is added to the mass of the cell by degrees, and that previously formed is pushed outwards. By the action of oxygen, and in consequence of other changes, the constituents are gradually resolved into bile, amyloid and fatty matter, which with salt constitute the principal "products" of the action of the liver-cell. Although any one who thinks over the facts and studies the general nature of the compounds which constitute the bile would not be very likely to suppose that those which were formed resulted in some mysterious way by some apparatus contained in the cell, the idea of some mechanism, the discovery of the structure of which would explain the formation of the constituents of a secretion, seems to have obtained

such firm possession of the mind, that attempts to discover something worthy of the name are still being made, while the belief in the existence of mechanism is so firm that it is almost a modern scientific creed that action depends upon structure, and that if only we could see the structural arrangement of an organ we should be able at once not only adequately to explain its action, but to artificially construct an apparatus which would perform precisely the same work.

The effort to generalize and establish great principles and new laws often results only in confusion of thought. The extraordinary longing to show that every principle and idea may be included in what has been called unity has led many to assert that the processes of nutrition and secretion are allied, inasmuch as every organ may be said to act towards others as a secreting apparatus. So every cell it is suggested may be regarded as a secreting cell. All nature might be called a field for secretion, life itself a secretion, and every class of living things a special secretion in relation to every other class. Nutrition and growth are undoubtedly common to every living particle, but the only use of the words secretion and excretion is to distinguish between that which is removed from the seat of its production to fulfil some useful purpose in the economy, from that which is to be removed from the body as quickly as possible. We must distinguish formed materials which constitute structure and take part in operations from matters which have nothing in common with structure, but which may consist of remarkable substances in solution or just separated from a solution.

It has always seemed to me that for the true explanation of the marvellous phenomena of formation and secretion we must look in an altogether different direction; so far as I can discern there is every reason to conclude that no mechanism, no arrangement of fibres, spaces, reticulations or other structural elements or arrangements that have been, or may be, found, will in any way account for the "action" of the cell. The all-important influence of nerve in regulating, in controlling, and in initiating actions of various kinds in living beings has, I think, absolutely nothing to do with the *formative processes*, either in respect of structure or chemical composition. These phenomena take place in many cases where nerve tissue exists not, and in many more at a period of embryonic life long antecedent to that when nerve organs and tissues begin to act. Of late years the so-called tendency of thought has glided in another direction, but the new theories will probably prove no more correct than the attempt to solve the mystery of the secretive process by attributing it to nervous action.

Like many ancient reasoners, some recent authorities have endeavoured to revive the old notion that action and the formation of remarkable chemical substances are due to structure. They maintain that if only we could ascertain the exact arrangement of the

structural elements of the cell-laboratory, we should be able to form an accurate conception concerning the precise mode of its action, just as in an ordinary laboratory we are able to account for the production of complex chemical compounds by the synthetical and analytical operations performed by the chemist. Observers have, therefore, studied with more and more minuteness the little cells concerned in the secerning operation in different organs in the hope of demonstrating some anatomical arrangements which have baffled all previous efforts, and which in a way correspond to the furnaces, the retorts, the alembics, the reagents, and the knowledge and manipulating skill of the chemist.

Karyokinesis is one new key by which the door of nature's laboratory is to be unlocked, but in the study of the phenomena included under this head, it is not too much to say that the real question has not even been considered. Admitting all as facts we are asked to admit, we shall find that we are not in the least degree nearer the knowledge of the actual changes which occur when, for example, biliary acids are formed from substances which by no other means known can be made to yield them, or compounds from which they may be obtained by further chemical action.

In order to demonstrate what have been called Karyokinetic figures, we are enjoined to proceed as follows :—To fix the tissues with absolute alcohol—then to stain safranin and transfer to a spirit and water solution of chromic acid—next to dehydrate with absolute alcohol, to clear up with bergamot oil, and to mount in dammar. "In this way the chromatic filaments and the true nucleoli are stained a lively red, the protoplasm and the intercellular substance remain uncoloured, the resting nuclei are faintly stained a pale red" (Dr. G. Martinotti and D. L. Resegotti in "Zeitschrift f. Wiss. Mikr.," iv, 1887, pp. 326–9.—From "Summary"—"Journal of R. Microscopical Society"—part 3, 1888, p. 516). Is the assumption that the appearances seen in a specimen which has been subjected to such operations are due to arrangements which actually existed during life in the slightest degree justifiable? Is it in accordance with facts hitherto ascertained concerning the phenomena of any form of bioplasm known to us to assume that, either as regards its actual structural arrangement or its chemical composition during life, the appearance of the dead matter affords the slightest clue as to the properties, relations, or actions of the particles or of the atoms when they were alive? Can it be possible to discover the nature of vital action in matter which has ceased to manifest vital action long before the examination was commenced? We might as well try to extract living mind from dead brain-pulp as to look for the mode of the working of the nucleus in figures, or fibres, or granules displayed in cells which have been subjected to such operations as those above recounted.

Many of the remarkable appearances which have been described and

figured by observers in recent years unquestionably show inequalities in texture, both of the formed material and living matter of the cell, and that of the nucleus itself in many cases. Many of the appearances have been figured with great care and accuracy, but it can hardly be said that they have helped to explain any of the phenomena of cell action. The interpretations which have been offered of the appearances observed do not lead us one step nearer the solution of the question of the mode of action of the matter which has been studied. The lines often seen passing from the circumference of the cell towards the nucleus are no doubt produced by currents of fluid passing towards the inner part of the matter of the cell and the nucleus, during life. While not a few of the lines and figures described in and about the nucleus are due to precipitation of matter from solution at the moment of death, others to changes induced in the fluid which was flowing just before death; and some of the means employed to render certain parts transparent, or to induce other alterations to facilitate observation, are no doubt accountable for some of the peculiarities described.

It has been assumed that peculiarities of the arrangement of some of the constituents of the nucleus will enable us somehow to account for the mysterious metabolic influence this part of the "cell" is supposed to exert upon matter around it. But it need scarcely be said that so far the precise way in which the fibres, or threads, or inequalities observed in certain cases, and under certain circumstances in and around the nucleus, or the induration, condensation, or molecular movements cause substances to be decomposed, and their elements to reunite in a peculiar manner to form special substances not present in the pabulum, has not been indicated. Nor has it been shown that the structural peculiarities in question are constant and universally present in all living forms and at every period of life and activity. Some argue as if the demonstration of anatomical peculiarities must necessarily lead us nearer to a knowledge of vital change, and, further, not a few infer that by future research arrangements of a structural character will be discovered, which will enable us to explain many of the changes which are at present inscrutable. But there is no reason whatever to suppose that structural arrangements of any kind ever have effected or will effect chemical decomposition or synthesis.

As far as I can see we might freely admit the existence of many times the number of peculiarities, anatomical, structural, or chemical, which have yet been demonstrated, or have been supposed by any one to exist, without our being in the slightest degree nearer any adequate explanation of the well-known facts. No physical, anatomical, or chemical differentiations in the world will account for the production of one particle of biliary matter or glycogen, or for the slightest movement of a particle of bioplasm. It is opposed to all that we know concerning the

changes in living matter to assume that any structural peculiarities demonstrated in the nucleus, living or dead, will take us any nearer to the discovery of its action than the homogeneity supposed to exist by a former generation of observers, or the mysterious differentiation powers assumed by their successors. It is ridiculous to attribute functional or metabolic power to passive membranous matter of extreme tenuity, which at least in many cases is undoubtedly formed at the moment of death or some time after that change has taken place, in reality all metabolic power having for ever ceased at the moment when death occurred. The above are a few among the many fancies authoritatively forced upon our attention for the purpose of bolstering up the shallowest and falsest doctrines ever sought to be imposed upon the credulous. So far, nothing that has yet been made out as regards the minute structure of any tissue or organ in any organism can be truly said to have enabled us to explain action. Nor could any one from a knowledge of the minute structure of a tissue say what was the exact kind of work it discharged. Even in the case of the nervous system itself, while we are enabled to trace the course taken by nerve-currents, and study the distribution of nerves to their minute ramifications and ultimate blending with the undoubtedly active substance, we have as yet learnt little concerning the nature of the nerve-current and the changes taking place at the seat of its source; while as regards the molecular phenomena preceding and attending the formation and arrangement of the substances constituting the matter in which nerve impulses are evolved we know nothing.

Not even the molecular movements or any of the remarkable changes which have been observed in connection with bioplasm or living matter enable us to form any conception of the real nature of the phenomena attending the simplest of its movements. It has not even been established that chemical change is necessarily or invariably associated with or preceded by mechanical phenomena.

Of all the strange theories advanced to explain formation, one of the most far-fetched and fanciful is that which assumes living matter to be a mere mixture of materials, the phenomena of which are due to the physical properties of its ingredients and which resemble those occurring in living matter. Such a view is absolutely untenable in the present state of our knowledge. It cannot be sustained for a moment unless well-known facts are completely ignored.

Strange indeed is it that several writers, disregarding the mighty difficulties which have been shown over and over again to preclude the acceptance of a purely physical view of life, and that grow more and more insurmountable as thought and observation advance step by step, still persist in proclaiming to be absolutely true what they cannot prove, and declare as certainly existing somewhere beyond their ken, that which

they admit exists not within the range of observation and experiment—the only sphere of action which they allow—exists at all.

Latest among declarations concerning life but supported by nothing save authoritative assertion, are those of Berthold, who hesitates not to assert that the forces determining the internal changes in a bit of living matter are one with those which cause fluid to assume the form of a drop or a stream, or cause it to spread out in a thin layer on flat surfaces, to "wet" one substance and recoil from another ("Studien über Protoplasmamechanik" by Dr. G. Berthold, Professor of Botany in the University of Göttingen. Leipzig: Arthur Felix, 1886. Review in "Nature," January 27, 1887, by H. Marshall Ward.)

Berthold informs us that Protoplasm is an "emulsion," and that oil globules, crystals, vacuoles, and other things which separate, do so according to the same principles as obtain in separations from lifeless mixtures. The "living substance of organisms" is according to this observer an extremely complex mixture of the inanimate,—a laboratory without a chemist, an engine spontaneously precipitated from the homogeneous without maker, designer, or driver to regulate its movement. Protoplasm, like Bathybius, according to this view, seems to be composed of many things, but in the language of Mr. Wright, in his review of the work, "it is active as a whole!" Berthold speaks of the "tendency" of a mass of protoplasm to assume a spherical form when in fact the "tendency" is for it to depart from the spherical form. It is dead not living protoplasm which tends to take the form of spherules like lifeless oil on water. The "amœboid condition" is said in the words of Mr. Wright to depend upon the degree of "wetting of the environment by the fluid protoplasm, and *vice versâ*." Pseudopodia are not actually protruded into the surrounding medium, but are "*drawn*" into it by the influence of the water. The water comes to the horse, not the horse to the water. The cart draws the horse not the horse the cart. Environment is active, the living thing passive. Heat, light, &c., excite; living mechanisms obey the stimulus, and respond. All this seems to me like the reasoning in a world long extinct, and of which the very existence is only proved by records which have been handed down to us.

Nothing is gained by calling protoplasm an emulsion, seeing that it is not like any ordinary emulsion that can be pointed out. It cannot, like an emulsion, be artificially made. No emulsion can do what every form of living protoplasm does. If living protoplasm is an emulsion, what is dead protoplasm; and if this is also an emulsion, what is the difference between the dead and living emulsion? Many specimens of protoplasm are perfectly clear, transparent, and structureless, as seen under the very highest powers of the microscope. Is there a single emulsion of which this can be said? If in a given form of protoplasm

granules or globules, crystals or other forms of solid, are visible, the *actual protoplasm itself is clear, transparent, and structureless.* If the solid particles are seen to move, the motive power is not in them, but they are passive and their movements are due to the inherent movement of the clear, transparent, structureless substance in which they lie.

It would indeed be more correct to say that the tendency of living matter was to assume various forms rather than the form of a sphere, at least while the protoplasm lives, than to assert that the last is its tendency. It passes into the spherical form when death occurs, or after death has occurred. The fact is easily verified by examining pus corpuscles, which are spherical in death, but exhibit the most diverse forms and active movements when living, a fact easily to be verified by any one who takes the trouble to examine, under a power of four hundred diameters or more, a little pus from the bladder in a case of catarrh of that viscus, when the urine is weak and not very acid, and contains comparatively little solid matter, within twenty-four hours of its escape.

In these days we look more hopefully than ever to chemistry for a full explanation of those cell changes which result in the production of the highly complex chemical compounds which form the chief constituents of many of the most important secretions, but for the arrangement of the atoms, for the placing them in position to unite and produce these compounds, life, not chemistry, is requisite. Among chemical changes there are none more remarkable than those occurring in the liver-cell which end by the formation of substances, the characters, properties, and composition of which are of the greatest interest. What is the active factor in these marvellous phenomena of a particle of a liver-cell? What are the necessary conditions of the rearrangement of the elements during the production of the compounds is as much beyond our present knowledge as is the question of the cause of the initiation or continuance of the movements of the matter constituting a particle of living bioplasm.

Nothing can be gained by speculations on the possible manner in which the properties of the component atoms of the bioplasm may determine the properties of the resulting formed products, because no facts that have yet been ascertained favour in the least degree the idea that the properties of a secretion or of any special organic compound are to be adequately accounted for by being referred to the properties of the elements of which these are composed. No knowledge of mere properties of elements would enable any one to build up in imagination a fraction of glycocholic acid. All that has been affirmed in this direction is not only pure conjecture, but for the most part conjecture advanced in spite of numerous well-known facts which have proved it

untenable from the first, and ought to have prevented it from being launched at all.

The first of the series of phenomena which results in the *formation* of any characteristic biliary compound is the selection and taking up by the bioplasm of the liver-cell of the nutrient pabulum from the portal blood as it traverses the capillaries of the lobule. That this is in solution, that this transudes through the capillary wall, that it bathes the surface of the cell, is admitted—but concerning the exact nature of the other events,—the selection of certain things, their precise course in the cell, and the manner of the change,—there is much difference of opinion. To my judgment, however, it seems to be proved that the fluid holding in solution matters out of which the characteristic products of the action of the liver-cell are formed passes through the outer part of the cell in many little streams, which converge towards the so-called nucleus. A solution of carmine certainly takes this course in the case of the liver-cells removed from the body of a recently killed animal. So quick is the flow through the substance of the liver-cell of the mouse, that the nucleus, as well as some of the matter around it, becomes tinted red in less than half a minute after it has been exposed to the action of the solution. Is it not, therefore, highly probable that certain constituents of the dissolved material traversing the cell are taken up by the nucleus and living particles around it, that is, by the bioplasm or living matter of the cell, which thereby increases in size? The new non-living matter passes into the living state and becomes "living." While in this condition the substances are changed. Their elements must be rearranged and probably for some time remain as it were in a state of suspension as distinguished from actual chemical combination. After some time the elements are caused to take up such relations or positions in respect of one another as will ensure that, when they pass from the living state into the condition of formed material, definite and often very highly complex substances result, which either directly or after further changes under the special conditions to which they are subjected become the matters to which the secretion owes its remarkable characters and properties.

In the changes which I conceive take place in the substance of the cell, the pabulum or certain of its constituents become living particles. These after a time die, and in dying or just before death the constituent atoms are placed in such positions that, the instant they are free of the constraining and suspending influence exerted upon them by the vital power, they rush together according to their chemical affinities, and combine and form the remarkable but non-living compounds in question.

The true cause of the production of the remarkable and charac-

teristic compounds must be looked for while the matter is actually in the living state, while the elements are being made to take those relations by which their special combination is determined. But the search is probably an impossible one in the present state of our knowledge, seeing that in such methods as we are able to pursue we destroy the life of the matter in the very first step of our investigation.

That some most powerful agency causes the elements to be arranged in a way which we cannot imitate, and under circumstances very different from those under which organic compounds can be artificially formed, is obvious. The agency in question is clearly powerful enough to decompose highly stable compounds, and to cause others as complex or more complex to be formed, and this at a temperature far below that at which any such changes can be effected in the laboratory.

The chemistry of the liver-cell is indeed complex, for very different classes of compounds seem to be formed at the same time; 1, matters which constitute the bile, and 2, matters which pass back into the blood to undergo still further change, while they circulate in the pulmonic and systemic vessels.

As already remarked, it has been suggested that the nucleus may somehow exert a metabolic influence, or in some way act upon the matters presented to the cell, as from a distance, by virtue of some mysterious metabolic agency which it possesses. But it seems to me that the facts adduced prove that soluble materials do actually pass into, and are certainly taken up by, the living matter of the cell, and caused to become living matter. This living matter gradually undergoes series of changes until it is at last converted into the constituents of which the "secretion" is formed. The chemical compounds constituting the secretion, therefore, result from the combination of elements whose arrangement prior to combination was determined by the power or property (vital) of the living matter, the action of which is evanescent, lasting only as long as the particular particle is alive. In this enquiry we are almost at once confronted with the fact that the clear, transparent, structureless living matter of cell and nucleus produces in dying or soon after death the characteristic compounds which cannot be artificially produced at the temperature of the body, or, under the circumstances, known to obtain in the organism. Neither will anatomical or chemical investigation in their present advanced state enable us to understand the means by which the result we know of is attained. Of the substances which almost seem to flash into being by the cell agency, some can undoubtedly be produced artificially; but how *absolutely* different are the conditions under which the same things are formed in the living cell laboratory! Since all living matter, as far as we are able to investigate it, has the same general appearance, and is structureless, while the formed

material resulting from the death of the living matters of different creatures, and of the different tissues and organs of the same creature, exhibits the greatest diversity of properties, composition, consistence, and durability, it follows that the determining cause of the latter differences must be associated with the living state. In other words, while living, the material particles are marshalled in such manner, and their elements made to assume such relations to one another, that the particular predetermined compounds shall certainly come into existence when the living matter assumes the condition of formed material, or after that change has taken place. One kind of living matter leads to the formation of one class of compounds, while another not differing from the first in any way we can demonstrate, produces, and at precisely the same temperature, and, at least in many respects, under precisely the same conditions, a totally different class of substances. In the laboratory how many very different processes, and what different forms of apparatus, will be necessary to form compounds differing from one another as much as fats and sugars and albuminous substances!

The force, then, which can alone be exerted in the living cell must be of such a nature that it can not only cause decomposition and disintegration of all sorts of compounds and separation of elements in combination, but can effect their rearrangement and reunion as compounds of the most complex character and often peculiar property which did not exist before, and which in many instances have never been produced in any other way. It may be that these or many of them will be artificially formed in the time to come; but, should this be so, we may feel quite sure that the method by which the production is effected will be of a kind absolutely distinct from that operating in nature under influences requiring no apparatus whatever, no active reagents, and a temperature not above 100°, and in many instances very much below that point. In short, no analogy exists between the natural and artificial chemical operation.

If we could ascertain exactly what was going on just before the living matter underwent conversion into biliary matters, even though we were not able to give an adequate explanation of the process, we should, at least, be able to surmise the general character of the phenomena which result in the formation of the characteristic constituents of the secretion. But, to form any accurate conception of the chemical analysis and synthesis or preparation for synthesis going on in the bioplasm, we must be able to study the living matter itself, and must learn something concerning the nature of the forces which determine the rearrangement of the elements when they are made to combine to form the substances in question. In the living matter itself the elements must be caused to take up certain special relations to one another, so that they must combine at the proper time and under certain

definite and prearranged conditions, to form the specific matters. We must enquire how material particles are constrained or forced to assume the relations in question—constrained and forced in spite of the tendencies of the particles themselves.

It is obvious that there must be some competent force or power which causes the elementary atoms to take definite positions, and in the exact number and at the exact distances from one another to ensure the end. No supposed properties, attractions, or repulsions belonging to the atoms themselves will account for this any better than the doctrine of chance or accident, which, however, the definite and constant composition as well as the remarkable individual and specific properties of the compounds compel us absolutely to discard. The force or power in question must indeed be far removed from any ordinary material forces and properties, seeing that it overcomes these just as if they existed not. It cannot emanate from matter, for might not matter exist, and does not matter exist, in infinite amount, and has it not existed for countless eons without any life or any manifestation at all resembling life? It will ere long be generally admitted that the assertion that matter implies life is one of the most monstrous and untenable of the many impossible propositions ever framed by ingenious but reckless speculators, and artificially and unfairly forced into notice.

Much that I have thought it right to consider in this and other works has a somewhat unpractical ring about it, but every one who thinks over the matter will, I am sure, agree with me in the opinion that medicine can only advance along the lines indicated. A knowledge of the chemistry of the liver-cell, even in its present imperfect and undeveloped state, does help us in a remarkable degree in considering the changes which we should try to bring about in departures from healthy action, and places vividly before the mind the dangerous consequences likely to result from its having to discharge more than its proper amount of work in a given time. Moreover, by trying to picture to ourselves what goes on as the cells grow and produce their remarkable products, we may reasonably hope, at least to some extent, to understand the manner in which our remedies, particularly such as iodide of potassium and mercurial preparations, may be taken up by the cell when brought in solution in the blood within the sphere of its action, and what they do when they get there. We may even be able to form some notion of the altered chemical cell action or change in the formed material induced by the drug to which its remedial action is due.

OF THE ULTIMATE RAMIFICATIONS OF THE FINE DUCTS, AND OF THEIR CONNECTION WITH THE CELL-CONTAINING NETWORK.

Anastomoses of the Ducts.—The anastomoses of the large trunks, and of the branches given off by the larger interlobular ducts, have been referred to, p. 49. They are certainly more numerous than, from the observations of anatomists, one would be led to suppose. The anastomoses in question, however, occur principally between the large trunks, as has been described. Different branches of the smallar ducts communicate with each other near the lobule where they eventually join the cell-containing network, but in some animals these communications between the smaller biliary ducts just prior to their reaching the cell containing network of the lobule are not very numerous.

The anastomosis of small interlobular branches of ducts coming from opposite points, according to my observations, is rare, as proved from careful examination of well-injected specimens of the livers of many different animals, but anastomoses between many lateral branches and subdivisions of the same fine duct are frequently met with both in the human subject and in many of the lower animals. In some cases, as in the pig, there is a network of very fine ducts which is continuous with the tubes of the cell-containing network, close to and apparently in part at least in the substance of the capsule of the lobule.

The smallest biliary ducts are directly continuous with the tubular network of delicate membrane in which the liver-cells lie; for, in favourable specimens, injection, forced in from the duct, has passed into every part of the tubular network, even quite to the centre of the lobule.* It is possible to inject the capillary network in the same preparation as that in which the ducts and cell-containing network have been injected. The reader will, I fear, find the evidence I shall adduce in favour of the above view tedious, but it is only by repeated observations in a number of different animals that one can hope to establish a fact so opposed to the conclusions of most writers upon the subject. Nor have I much hope, notwithstanding the evidence I have adduced, that the correctness of my observations will be admitted at present, though I feel confident that eventually the conclusions at which I have arrived will be confirmed and fully borne out by future investigators.

As already remarked, many of the fine ducts which come off from the trunks are connected by smaller branches, which arise not far from the point at which they are given off, as represented in Pl. V, Figs. 11 to 14. I have been able to prove, from many successful injections, that these

* In this work the word "*duct*" is used to denote the tubes which carry off the secretion, in contradistinction to the *secretory tubes*, or "*cell-containing network*" in which the secretion is formed.

communications are very numerous indeed. Similar anastomoses occur to some extent in the case of branches of moderate size in the portal canals of the human liver; and in very good injections small branches coming off from a trunk at short intervals may be seen to communicate freely with the trunk itself, and with each other, by numerous intermediate branches, so that a network is formed at a short distance from the parent trunk. The meshes of this network are most variable in size and shape, and the tubes are more dilated in some places than in others. Some of these branches are composed simply of delicate membrane and epithelium, but the largest have a fibrous coat, though it is generally much thinner than that of the duct itself. Branches of the vein and artery, and of lymphatics (in the case of the larger portal canals), ramify among these ducts, and lie in the meshes of the network. In very good injections this network of branches of the duct is demonstrated in the adult, but in the fœtus the communications are to be shown with less difficulty, although the branches are not so tortuous and are less complex, Pl. VII, Fig. 20, p. 50.

The smallest branches of the duct may be readily followed, in tolerably good injections, to the surface of the line of hepatic cells, which bounds the portal canals, and not unfrequently they may be traced among the tubes of the cell-containing network, in the human and other livers. In the pig, however, the trunks may be seen gradually breaking up into their smaller branches, which run upon the capsule of the lobule, and which appear to anastomose only very rarely, as above remarked. In the human liver an irregular network, in good injections, is to be demonstrated close to the larger branches of the ducts, and might be termed an *interlobular network*; but the arrangement is certainly not universal, nor does it seem to me to be sufficiently extensive to render it desirable to give it any special name. I have not been able to demonstrate it in the pig, seal, rabbit, horse, cat, or monkey, though I am not prepared to affirm its absence in these animals, as it may exist here and there in parts of the liver.

It may be stated generally, that small branches of ducts carry off the secretion from that part of the lobule to which they are distributed These small branches unite to form slightly larger ones, and these, again, to form others. *The smallest branches sometimes pour their contents at once into interlobular branches; in other cases they are connected by a few transverse branches,—and sometimes they form an irregular network before they are connected with the interlobular ducts.*

I think the extent of this narrow ductal portion of the cell-containing network, as it might be called, varies considerably in extent at different times in the same liver. It is small in extent or can hardly be demonstrated at all in the liver of the young, while it increases as age

dvances. In cases where the liver-cells undergo degeneration, as in cirrhosis, there is no difficulty in demonstrating a network of considerable extent, extending half way perhaps to the centre of the lobule, the tubes of which contain small cells which do not form secretion. In an animal like the pig, whose digestive physiology is of the most active kind, the liver-cells grow larger or smaller within a very short period of time. In a pig that lives upon very little food for a considerable time, this ductal portion of the cell-containing network increases in extent, while if the liver-cells grow and discharge active work they occupy a greater portion of the tubes and the very narrow portion of the network is reduced in extent. In this animal each individual lobule may undergo great change in dimensions, without any of its constituent tissues being deranged. Its cells may increase or decrease in size and number many times in the course of life without the liver undergoing any pathological changes. The *ductal* network exists in the most perfect form in the liver of the pig when the organ contains little fat, Pl. XIX, Fig. 59. When, on the other hand, the liver is fatty, this network is distended with ordinary hepatic cells containing much fat and free oil globules in considerable number. So that it seems probable that under certain circumstances the ductal network may contain secreting cells, while under other conditions the superficial part of the cell-containing network may become altered and exhibit the characters of the ductal network.

OF THE FINEST BRANCHES OF THE DUCTS IN MAMMALIA.

It has been already stated that in injected preparations the smallest branches of the ducts can be traced up to the liver-cells. The walls of the small ducts are composed entirely of very thin membrane, which, at least in many cases, is lined with epithelium which differs in character from the liver-cells, being of a columnar or sub-columnar form. But often a transition may be observed from the secreting to the ductal epithelium, and it even appears that at least up to a certain period of the life of the cell, it might ultimately attain to the condition of a secreting cell, or continue in the lower character of mere ductal epithelium with no special function. The minute thin-walled ducts do not always lie in such close contact with the smallest branches of the vein, as is invariably the case with the larger trunks. The manner in which the finest ducts join or are continuous with the cell-containing network of the lobule is by far the most important point in connection with the anatomy of the liver.

Some of the finest branches of the duct often appear to lie amongst the most superficial portion of the cell-containing network without

being immediately connected with the tubes or cells in this part, but they may be followed for some distance, and may be seen to join a portion of the network which lies at a deeper part of the lobule; the tubes at the superficial portion of the cell-containing network being continuous with small ducts which pass a short distance through the superficial layers of the cell-containing network, to join tubes situate some distance below the surface of the lobule. This point is well shown in a drawing of the seal's liver (not published in this work), where two ducts are seen to join the superficial part of the network, and another in the lower portion, is observed passing for a short distance amongst the tubes of the cell-containing network, to be connected with tubes some distance from the surface. One of these penetrating branches has been figured by Gerlach, and, as he very justly observes, these branches are much narrower than the cells between which they lie, and hence he concludes, very properly, that they cannot contain liver-cells. He supposes, however, that the fine tubes in question terminate by open mouths, into which the bile passes from narrow interspaces between the cells; but this view is, I think, altogether untenable, as I shall endeavour presently to show.

In the pig, numerous fine branches having reached the surface of the capsule, perforate it, and are immediately connected with a dense network, forming the most superficial portion of the cell-containing network, and consisting of very fine ducts, the tubes of which often contain small cells, granular matter, and perhaps oil-globules, but usually no secreting cells of the ordinary size are to be found within them. The diameter of these tubes, which ramify in and below the capsule, is of course much less than at a greater distance within the lobule. When the liver is very fatty, however, some of the tubes of this part of the cell-containing network contain very many cells filled with oil-globules, as is shown in Fig. 49, Pl. XVI, in which the *very narrow ductal portion of the tube is seen to dilate considerably at the point where it contains liver-cells.* The epithelial cells in the duct can sometimes be traced quite up to the point which distinguishes the *efferent duct* from the *secreting portion* of the tube. This is well shown in the figure at *b* and *d*, which was taken with the camera from a preparation which demonstrates these interesting points very clearly. The narrow ducts, and the wide secreting tubes, both contain a very little injection; and, in consequence of their accidental isolation from adjacent parts of the network, their continuity is distinctly seen. The delicacy and extreme narrowness of the ducts will readily explain the difficulty of demonstrating the exact point where they become continuous with the cell-containing network; for in preparing specimens the tubes almost invariably break at the constricted portion, when an attempt is made to isolate them; while, if the part in question cannot

be well isolated from the adjacent tissues, it will be impossible to prove that the arrangement really exists. In some preparations, by an unusually lucky accident the cell-containing network breaks, instead of the very narrow portion of the duct giving way, and not unfrequently this tender spot is protected, as it were, by lying upon the walls of a branch of a small artery or of the portal vein.

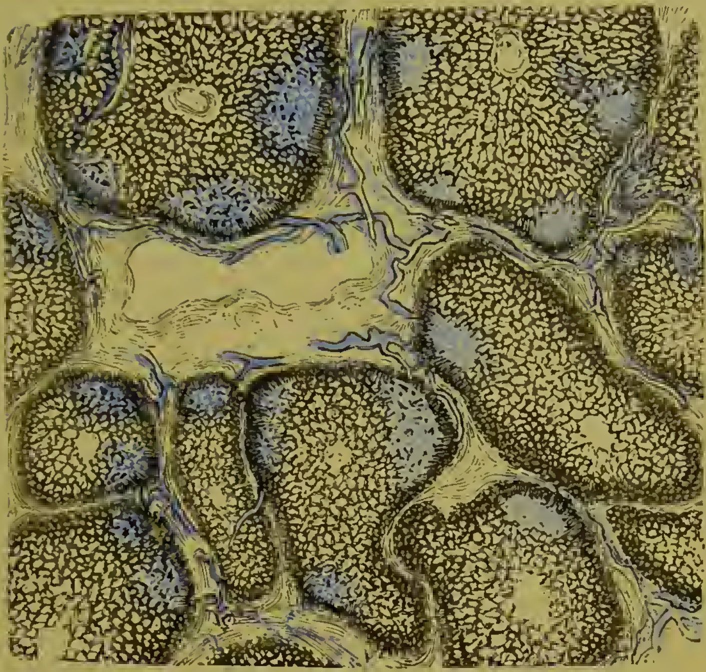
The further continuity of the ductal portion of the network with the tubes of the cell-containing network is shown by dotted lines, Fig. 49, Pl. XVI, at *b*, *c*. I have seen the same point in several specimens, but never in one which shows a greater number of minute ducts, and their points of connection with the tubular network in which the secreting cells lie, with greater distinctness. These narrow ducts are only 1-3000th of an inch in diameter; while the expanded portion, in which the liver-cells lie, and with which they are immediately continuous, is upwards of 1-1000th of an inch in width.

In Fig. 66, Pl. XX, is shown a similar arrangement in a portion of human liver, which had been treated with soda, and kept for some time in strong syrup. Here the epithelium of the ducts is well shown, but the specimen has been flattened somewhat by the pressure of the thin glass. Fig. 67 is a representation of another section of the same liver, which has not been subjected to pressure, in which the *narrow ductal part* of the tube at *a* contrasts remarkably with the *wide secreting portion* continuous with it. In the human fœtus, the connection between duct and cell-containing network is shown in Pl. VII, Fig. 20, at *a*, and in Fig. 21 it is represented in the liver of the calf. In the seal the hepatic cells are small, and injection readily passes into the tubes which contain them. The small ducts are comparatively few in number, but their course in this animal is very easily traced, and they can be well seen through the thin wall of a small portal vein which has been injected with clear size. In Fig. 50, Pl. XVI, p. 112, the connection between the ducts and the cell-containing network in the liver of the seal is well represented. The portion of the cell-containing network lies upon the surface of a small branch of the portal vein.

The view of the arrangement demonstrated in these drawings of the ducts and their continuity with the cell-containing network of the lobules, and held to be constant in man and animals, is quite incompatible with the conclusions now generally held and taught, and which are supposed to result from the fact having been established by injection that the bile ducts really begin in a capillary biliary network of excessively fine tubes, which are in very close relation with individual hepatic cells. The appearances which have led to the acceptance of this view may, however, be explained in another way. By skilful management and very slight pressure a little of the injecting fluid is caused to pass along the slight spaces left between the liver-cells and those between the

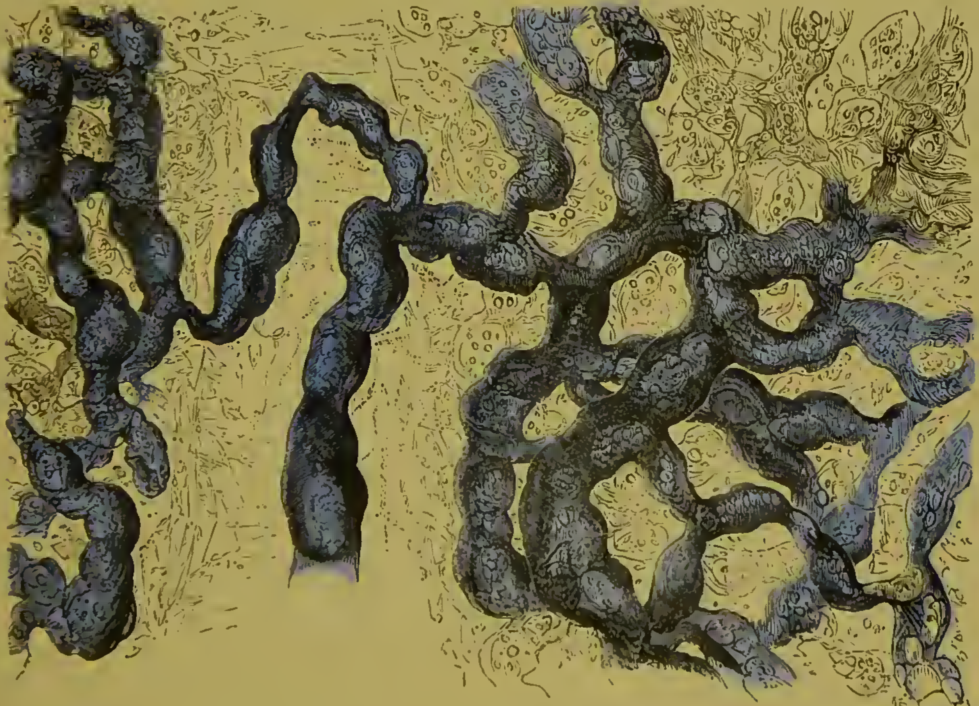
MINUTE DUCTS OF THE HUMAN LIVER INJECTED.

Fig. 41.



Thin section from the liver. Ducts injected blue. The injection has passed into the tubes of the cell containing network, the walls of which in this case were thicker than usual, while the tubes were narrower. × 20. p. 109.

Fig. 42.



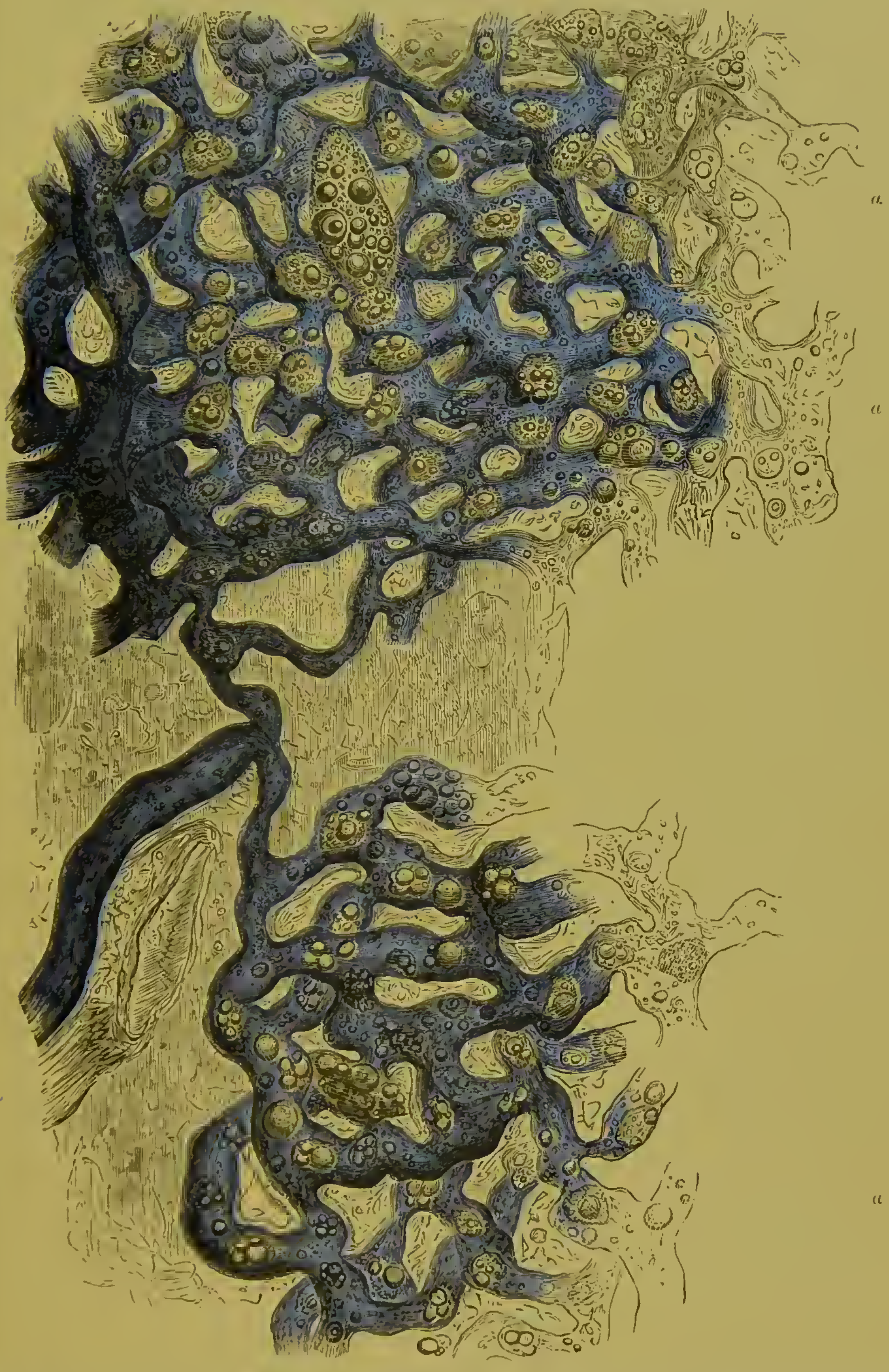
A small terminal duct in an interlobular fissure, and portions of two adjacent lobules from the specimen represented in Fig. 41, but magnified 215 diameters. The tubes of the cell containing network very distinctly seen. p. 109.

L.S.B.

[To face page 101.

FINEST PORTION OF THE DUCT AND ITS CONTINUATION AS THE LOBULAR NETWORK OF THE HUMAN LIVER.

Fig. 43.



A small terminal duct of the human liver, dividing into two branches, each of which becomes immediately continuous with the cell containing network of two adjacent lobules. The "cells" of the network at the margin of the lobules contained a great number of oil globules. The injection has surrounded many of the cells The outline of the walls of the tubes of the cell containing network can also be seen in the uninjected portion of the tubes at *a*, *a*. *b*. A small branch of artery. × 215. p. 109.

L.S.B

[To follow Plate XII.

latter and the walls of the tube in which they lie. Moreover, as the specimens which show the appearances in question have been mounted in Canada balsam, the injection in the interspaces will have undergone some shrinkage during the preparation of the specimen, and thus the resemblance to a network of very fine tubes becomes still more marked. If, however, more of the injecting fluid had been introduced and under greater pressure, the wide tubes of the cell-containing network represented in my drawings would have been distended, and many of the cells completely surrounded with injection, Fig. 65, Pl. XX, and the appearances represented in many of my drawings would have been produced. And further, it must be borne in mind that in the preparation of thin sections in the manner now generally adopted, several layers of the cell-containing network are included in the section which, however, being mounted in a very highly refractive transparent material, does appear very thin, and consequently when the specimen is placed in the microscope we see several layers of hepatic cells, without being able to isolate one layer or one cell. In this way we seem to see a far larger number of small ducts ramifying over a given area of hepatic structure than really exists, and it is not wonderful that appearances leading to the inference that many fine ducts are distributed to each individual cell should be produced.

After the appearance of a memoir by Budge, of Bonn, in 1859, I succeeded in preparing specimens illustrating both views of the anatomy of the organ from the very same liver, and I cannot therefore accept the interpretation of the fine lines of injection seen around the cells, which has been widely accepted in Germany and in this country. No doubt those opposed to my view will urge that the appearances obtained by me result from *over-injection of the minute gall-capillaries and their rupture;* but, if that supposition was true, the appearances would have been very different from those seen in my specimens. For instead of *distinct tubes with well-defined outlines directly continuous with the ducts, and in many instances capable of isolation from the capillary vessels*, the intercapillary space would have been entirely filled with the injecting fluid. Now, I have actually filled these intercapillary spaces, and the difference between such a preparation and the specimen in which the cell-containing network has been properly injected is so great that it is impossible to mistake the one for the other. If the reader will refer to the injection of the capillaries in Fig. 46, Pl. XIV, and consider what the exact complement of this would be, I am sure he will agree that the appearances would be widely different from those seen in Fig. 43, Pl. XIII.

But the advocates of the minute gall-capillaries have another difficulty, of the existence of which many are evidently quite aware, though they do not direct attention to it. In the drawings illustrating

their views, the arrangement of the marginal cells of the lobule of the liver, and the precise relation of the interlobular ducts to the supposed minute "gall-capillaries" is not clearly indicated. Take, for example, Hering's article upon this subject, in "Stricker's Anatomy," Part III; is it not remarkable that the author does not give the student the benefit of *one single drawing showing the connection between the interlobular gall-ducts and the gall-capillaries of the lobule?* This is the point above all others upon which clear and positive information is desired, and the one to which I attached the greatest consequences in my own investigations in 1854. The arrangement of the secreting structure of the liver cannot be decided unless this part of the course of the duct is conclusively demonstrated; and, considering the numerous figures given in my memoir to illustrate this special point, it seems strange that it should have been so neglected by subsequent investigators. But a careful comparison between Hering's Fig. 123, "Stricker's Anatomy," Part III, p. 445, and several of my own (20, 21, 29), in Pl. XV of the "Phil. Trans.," 1856, should be made. At the upper part of Hering's figure on the left hand, is seen the point where the cells of my cell-containing network are gradually becoming drawn out and modified, to become continuous with the finest duct. No wonder Hering remarks upon the obscurity connected with the demonstration of the transitional forms of epithelium supposed to exist between that of the ducts and of the secreting part of the liver.

The preparations which are represented in Pls. XII, XIII, and in Figs. 45, 46, 47, Pl. XIV, were obtained from a human liver, the ducts of which had been very successfully injected with the Prussian blue injecting fluid (the composition of which has been given in "How to Work with the Microscope"), very soon after the organ had been removed from the body. The injection of the duct was fortunately completed without the occurrence of rupture or extravasation. The capillaries were separately injected from branches of the portal and hepatic veins, while into some of them which were larger than usual some Brunswick black was accidentally permitted to run in after the specimen was mounted and the cover-glass cemented by that substance, Pl. XXIII, Fig. 79. The tissues of this particular liver had been rendered firmer, and, therefore, more favourable for investigation by slight morbid change. In consequence of long-continued mitral obstruction, the blood had distended the large veins. The branches of the hepatic vein and the corresponding capillaries near the centre of the lobules were found to be distended to nearly twice their normal diameter, and consequently the *tubes* of the cell-containing network lying between these had suffered compression, and were much narrower than usual, Fig. 75. But the same condition of venous obstruction had led to another change, to which the success obtained in making demonstrative specimens from

this liver may be mainly attributed. The walls of the capillary vessels, the minute ducts, as well as the tubes of the cell-containing network, were all thickened, and without being fibrous or opaque, were much firmer than in the healthy state. This change was advantageous for my investigation, not only because the tubes effectually resisted the pressure employed in injecting, but the delicate textures supported one another. The thin-walled capillaries, from the greater firmness of their walls, preserved their previous condition, and when a section was made, remained open, and their relation to neighbouring tubes was rendered thereby most clear and distinct. Moreover, the entire hepatic tissue was much firmer than usual, and exceedingly thin sections could be obtained in any part of the liver, and in any direction, without the usual difficulty. And the cells themselves, being firm and somewhat condensed, remained in their natural position when sections were made from the fresh liver, and were not smeared over the freshly-cut surface of the section by the action of the knife. The previous hardening of the tissue, so strongly advocated in cutting thin sections of the liver, cannot be carried out as part of the method which I have been led to adopt, and the thinnest sections prepared by hardening are thicker than those obtained by my plan, and, although the latter is very difficult to carry out, is attended by many failures, and requires great patience; when one does succeed, the specimen is really demonstrative.

My specimens were mounted in the strongest glycerine, to which a little acetic acid had been added. I have several excellent preparations from this liver, which have been preserved for years, and some of the drawings of injected ducts and cell-containing network represented may yet be compared with the actual specimens from which they have been copied. The preparations I have figured were selected from a great number, but there was no difficulty in finding many pieces in which the same facts could be demonstrated, though in a more limited extent of tissue.

The appearances seem to me to conclusively prove that the view concerning the structure of the liver to which I was led before the year 1855 is correct. Upon this view alone, I believe can the facts demonstrated in my specimens be explained. If the injection has not passed from the interlobular ducts into a network of tubes in which the liver-cells are contained, where is it? The cells are certainly surrounded, and coloured by the injection which as certainly is contained in the cavity of a tube, the outline of which can be seen in many places most distinctly; and this outline is separate from that of the vessels. Even by the aid of low powers the tubular arrangement of the secreting structure can be well seen at various points at the margins of the lobules where the structure happens to be well injected, Pl. XII, Fig. 41, but when some of these spots are examined with a quarter of an

inch object glass, it is not possible to doubt. With the aid of a twelfth magnifying 700 diameters, the outlines of the tubes of the cell-containing network can be seen, and the excessively thin membrane may be demonstrated in situations where the injected material exhibits interruptions.

In the figure in Pl. XIII, the fine duct distended by injection is seen to divide into two branches, which soon branch so as to form the cell-containing network of the lobules, and this can be followed quite to the centre. Not only can the hepatic cells be seen with the injection in the interior of the tubes in contact with them and surrounding them, but the injected portion of the tubes can without difficulty be traced onwards into that part which has not been penetrated by the injection. *See* also Pls. XII and XIV. The continuity of the walls of the tubes can be traced with the aid of a high power even to the central part of the lobule, Pl. XX, Fig. 68. The specimen represented in Pl. XIII is a very important one, because the arrangement is not only very distinct, but it is displayed over an extensive area. This section was an unusually fortunate one, obtained from the surface of a small branch of the portal vein, upon which the part of the duct and cell-containing network figured was lying. As the hepatic cells at the margin of the lobule contain numerous oil-globules, which are very distinct, not the slightest doubt can be entertained as to their position, or as to their being surrounded by the Prussian blue injecting fluid.

What other interpretation can be given of the appearances here indicated? Is it possible to entertain any other view than the one I have adopted? An opponent might of course deny that my drawings are accurate, but while the specimen remains to be compared with the representation, denial would be useless. It has already been so compared by a number of observers.

No compromise as regards the question at issue is possible. If the view now generally entertained in Germany is correct, my conclusions are erroneous. It is of course impossible that both views can be accepted, and it is now quite time that an anatomical point of this kind should be set at rest. Until this is effected, little real progress can be made in determining the changes taking place in the liver in disease. I beg the reader, while examining my drawings, to put to himself the question, Is it possible to explain the appearances delineated upon the supposition of the existence of cell-surrounding and cell-penetrating minute gall-capillaries? Those who still insist upon this view are, in fact, compelled to altogether deny that I have seen in my preparations what I have figured and have shown to others. But while my opponents cannot account for the facts demonstrated by me, I am not in a position of like difficulty, as regards the explanation of the appearances which are unquestionably to be obtained by the method of proceeding recom-

mended by them ; indeed, such appearances are seen here and there in all injected livers, but the uniformity of results so commonly obtained in the case of the liver of the rabbit is not met with in all vertebrate animals. The appearance of very minute ducts (gall-capillaries) surrounding the cells arises, I believe, simply from the injection having been introduced under very slight pressure, having in consequence only made its way into the narrow spaces between the cells and in the intervals between these and the walls of the tube.

I will now beg the reader to carefully examine several of my drawings which illustrate the distribution of the finer hepatic ducts and their communications with the tubes of the cell-containing network in order that he may have before him the most important of the anatomical evidence which has influenced me in my conclusions concerning the minute structure and action of this most important gland, by the agency of which in a given time is chemically changed an amount of material far exceeding that acted upon by all the other glands of the body put together.

In Fig. 41, Pl. XII, a thin section of human liver magnified twenty diameters is represented. Parts of a dozen lobules are seen, and in many interlobular spaces several fine ducts over-distended with injection may be traced into the adjacent lobules where they become continuous with the cell-containing network. Below, in Fig. 42, a portion of the same section is shown magnified two hundred diameters. A fine terminal duct, fully distended with Prussian blue injection, is seen to divide into two branches which are seen to be directly continuous with the tubes of the cell-containing network of the lobules, which ramify on several different planes. In many situations the injection is seen to cease abruptly, while the outline of the tube can still be followed for some distance in the uninjected portion. Many of the cells are also distinctly shown both in the injected tubes and in those portions of the tubular network into which the injection has not penetrated.

A still more remarkable specimen is the one already referred to in Fig. 43, Pl. XIII. No one who has seen these preparations has suggested any other interpretation of the appearances than the one here given. Nor do I think that any reasonable explanation other than the one given can be found. That such specimens as these are seldom to be met with is not surprising if one considers the softness of the texture and the difficulty of obtaining a section not much more than one five-hundredth of an inch in thickness, without disturbing the relation of the several component structures to one another, and of transferring the specimen to be mounted in syrup, glycerine, or some such medium that readily mixes with water.

The drawing is worthy of attentive examination. It is an exact copy of the specimen, which is still in my possession, and, although

more than twenty-five years have passed since it was prepared, during which time it has been preserved in strong glycerine, it still shows the points represented. The outlines of the tubes are as distinct in the specimen as is shown in the drawing, and it is difficult to understand how there can be any doubt whatever as to the true arrangement of the secreting cells and their relation to the ducts. The injection can be seen around the cells, some of which contain many large oil-globules, and in several situations it has penetrated a certain distance and then ceased abruptly close to a cell. The outline of the tube can be seen and followed with certainty, and the cells are seen in it to the left of *a* in the drawing. Although the section is exceedingly thin, the tubes of the cell-containing network represented really occupy many different planes, and by carefully focussing their sinuosities can be followed without difficulty.

The clearness with which all the above points can be demonstrated is due to the fact that the thin section has been removed from the surface of a small branch of the portal vein, the membranous wall of which has prevented the tubes from being stretched or unduly pressed; their relative positions have in consequence been preserved as in the natural state of the part.

The reader will observe that that portion of the duct which is directly continuous with the cell-containing network, and which is so difficult to demonstrate, is here clearly seen. No doubt it appears larger than it is in nature owing to being distended with injection.

Another specimen, magnified only a hundred diameters, taken from the same liver in which the connection between the finest duct and the tubes of the cell-containing network is well seen, is also given in Fig. 47, Pl. XIV. Fig. 45 is from another human liver. The terminal duct and its subdivisions are very clearly seen, and several ramifications can be traced with certainty to the cell-containing network. The cells are somewhat shrunken but are seen very clearly, many being completely surrounded by injection. In Fig. 46 the capillaries have been injected, and it is intended to illustrate the fact that in all parts of the tubes the cells lie within tubes and do not entirely occupy the intercapillary spaces.

Sometimes the Prussian blue injection runs into the tubes of the cell-containing network very readily, perhaps in consequence of the cells having been more or less contracted and shrunken at the time the animal was killed. An excellent specimen of this is represented in Fig. 44, Pl. XIV, on the surface of the liver of the rabbit. A very thin section was taken from the convex surface without removing the peritoneum. The tubes of the cell-containing network are here exceedingly distinct, and on the left side of the drawing a very fine duct is seen. In many places the injection has not run into the tubes of the

network, so that the cells as well as the outlines of the tubes can be very distinctly seen. The bioplasm of the cells is coloured red.

Another remarkable and clearly demonstrative specimen from the rabbit's liver is represented in Fig. 48, Pl. XV. The clearness with which the network of finest ducts and the direct continuity of these with the cell-containing network was seen is due to the fact that the part selected was lying on the surface of a small portal vein which had been well injected with transparent gelatin. The terminal branch of the duct is distended almost to bursting, while the tubes of the network are well seen lying on different planes as they ramify over the surface of the thin transparent walls of a small branch of portal vein injected with clear gelatin.

In Fig. 50, Pl. XVI, below the drawing of the ducts and their connection with the cell-containing network of the pig's liver, and described in p. 103, is a corresponding preparation from the liver of the seal. The fine terminal duct is seen ramifying upon a small branch of the portal vein which had been injected with colourless size. By its side is a small branch of the artery. The commencing portion of the lobular cell-containing network is well seen, and the relation between the tubes containing the cells and the capillary vessels is shown.

DUCTS IN BATRACHIA.

The direct continuity between the ductal portion of the tubes and the tubes of the network containing the secreting cells is very clearly demonstrated in the frog's liver, Fig. 51, Pl. XVII. It is true there is often a difficulty in causing the injection to reach the tubular network in consequence of the subcolumnar epithelium of the ducts being detached here and there and accumulating in the narrowest parts of the tubes. By using very slight and prolonged pressure, especially in the case of animals in the latter part of winter when the liver has been inactive for many months, a satisfactory injection may generally be effected. In many of the interlobular fissures the ducts are numerous and very distinct, and can be traced on to the cell-containing network very distinctly. The tubular network does not branch so freely as in the liver of mammalia and birds. In some cases a gradual change in the character of the epithelium may be observed as we pass from the finest ducts to the cell-containing network, Pl. XIX, Fig. 57.

Some of the ducts and their connection with the tubes of the cell-containing network of the liver of the newt (*Triton cristatus*) is well seen in Fig. 71, Pl. XXI, p. 116.

In the liver of the toad I have not only succeeded in making satisfactory injections, but have obtained many specimens showing the arrangement of the finest ducts and their continuity with the cell-

containing network so clearly as to leave no doubt whatever on the mind. Moreover, I have been able to obtain many fine ducts with diverticular appendages or follicles containing a number of large secreting hepatic cells. These diverticula, Pl. XVIII, Figs. 53, 54, 55, 56, very closely resemble the arrangement seen in many of the mollusca, and compare well with those connected with many of the ducts in the transverse fissure of the human liver and with some of the ducts of the pig's liver.

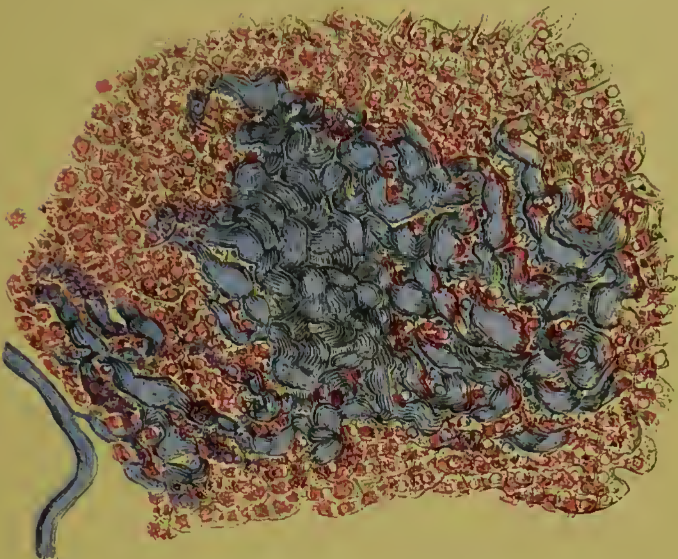
Many of the diverticula or hepatic follicular glands, as they might well be called, of the batrachian liver exhibit a lobular appearance, and very frequently the division extends to some depth, so that we have an arrangement of follicles opening into a duct very closely resembling that existing in the salivary and labial glands.

A still more interesting fact is to be noticed with regard to some of these elementary portions of the toad's liver. The follicles themselves are evidently undergoing further division, and in some cases this occurs to such an extent as to give the appearance of a network like that seen in the mammalian liver.

In Pl. XVII, Fig. 52, I have figured a very remarkable specimen. The entire collection of tubular follicles being isolated and embedded as it were in a thin layer of connective tissue and uncomplicated by the presence of capillary vessels, there can be no question whatever as to the exact arrangement. Indeed, if to the layer of cell-containing tubular prolongations shown in Fig. 52, Pl. XVII, we conceive one or two more, we should get an appearance exactly resembling that seen in a thin section of the mammalian liver. In the preparation of the toad's liver from which the drawing was taken, one can see in many places indications of the tubes giving off, as it were, lateral buds, which gradually extend and form tubes from which further lateral diverticula proceed. This, I believe, precisely corresponds with the changes which take place in the liver of the mammalian fœtus, and which occur but more slowly during the early years of life. In the central part of the lobule of the mammalian liver it is probable that new tubes of the cell-containing network are formed in healthy organisms, even in adult life. In certain forms of cancer this same kind of growth takes place, but so very rapidly that the extensions grow irregularly and invade one another, some being destroyed and caused to waste by the pressure exerted by the latest growth, which in its turn succumbs to the more rapidly growing diverticula which succeed.

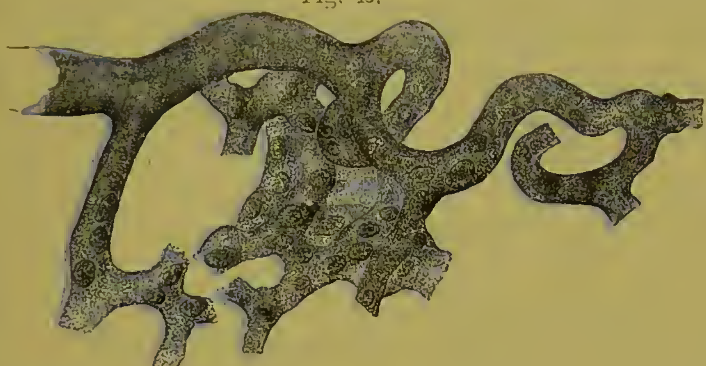
It is demonstrated by these observations not only that the tubes of the cell-containing network are directly continuous with the duct, but that these are formed by diverticular extension of the already developed tube. A small bulge appears at a part of the duct, and this gradually increases until a small follicle-like dilatation is produced, which still

Fig. 44.



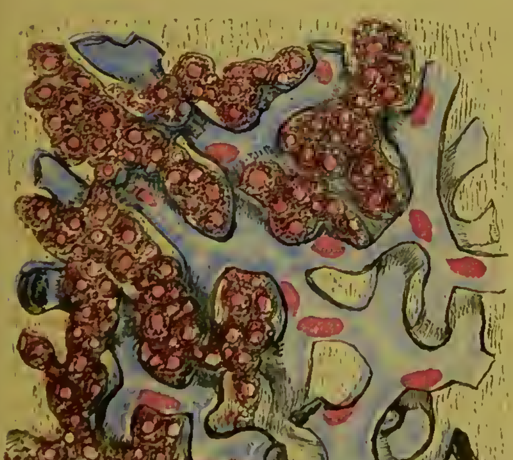
Surface of the liver of a young rabbit, the duct of which had been injected with Prussian blue fluid. The tubes on the surface just beneath or actually in the substance of the capsule contained very few cells, and in consequence the tubes are fully distended × 125. p. 110.

Fig. 45.



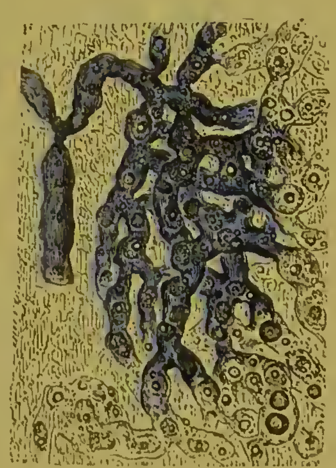
Small duct from the human liver at the point where it is continuous with the cell containing network. The duct is distended with injection which has surrounded the cells in the tubes of the network. The latter are altered in character by the injection. × 150. p. 110.

Fig. 46.



Cell containing network and lobular capillaries with their nuclei. From the human liver. × 200. p. 110.

Fig. 47.



Small interlobular duct and portion of cell containing network showing the injection amongst the cells. Human liver. × 100 diameters.

L.S.B., AD. NAT. DEL.

[To face page 112.

FINEST DUCTS.—LIVER OF RABBIT.

Fig. 48.

Interlobular duct of rabbit's liver, injected with Prussian blue fluid. The duct lies upon a small branch of the portal vein, which was injected with plain size. The duct is unduly distended with injection, but the continuity between the finest branches and the cell-containing network of the lobule is well seen. The liver cells were very small, and many had undergone disintegration by disease, consequently the injection penetrated farther and more freely than usual. × 215. p. 111.

L S.B., AD. NAT. DEL., 1854.

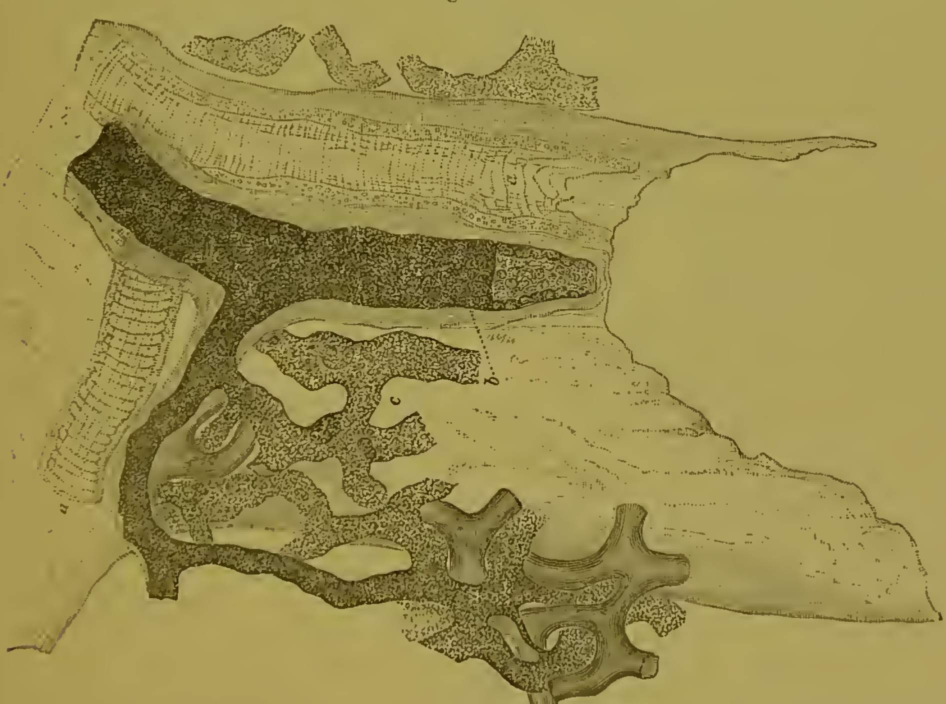
[To follow Plate XIV.

FINEST DUCTS.—LIVER OF PIG AND SEAL.

Fig. 49.

Connection between duct and cell-containing network as proved by injection. *a* Small trunk, giving off severa branches. *b* Distended by injection which has reached and entered the cell-containing network. In many places the outlines of the cells can be very distinctly seen, although they are surrounded by the injection. × 215. p. 103.

Fig. 50.



From a small portal canal of the seal's liver. The large vessel is the *portal vein* which had been injected with gelatine. *a* is the *artery* uninjected, showing the circular muscular fibres very distinctly. *b* The *duct* injected with *Prussian blue*, which has filled the finest ducts, and passed into the cell-containing network *c*. The individual liver cells were not defined in the specimen, and the tubes seemed to be filled with granular contents, in which only here and there could indication of division into cells or separate portions be made out. × 215. pp. 104, 111.

L.S.B., AD. NAT. DEL., 1854.

[To follow Plate XV.

growing away from the duct gradually becomes more and more complicated by the formation of new extensions, until at last the appearance represented in Fig. 52, Pl. XVII, results. And it is impossible to say why any given diverticulum appears at a particular part of the duct or tube already formed, or why, of numerous diverticula found in certain cases, one only here and there gives origin to tubes of cell-containing network. From these specimens it seems to be certain, however, that the secreting tubes of the liver do not originate in a new centre outside the duct, which eventually opens into it, but from the budding out of the duct itself, and that the epithelium undergoes slow change in the diverticulum that is formed, and gradually acquires the bile-forming power. Sometimes it seems to be the ductal epithelium which becomes gradually modified as growth and multiplication occur until elementary parts are formed, from which well-formed secreting cells proceed; while in other cases the ductal epithelium ceases so abruptly where the secreting epithelium begins, that it is difficult to believe there is, or has been, any intimate relationship between the two kinds of cells, and one would be rather inclined to infer that the secreting epithelium grew from germs distinct from those which gave origin to the epithelium of the ducts.

The little diverticulum having formed on the side of the duct, liver-cells begin to form within it, although these are totally different from the ductal epithelium which from the mode of its formation the diverticulum would probably include. It would seem that from one or more of the included cells germs were produced which had a wonderful power of growing and multiplying, and producing cells very different in properties and appearance from themselves and the cells from which they sprang. This is a very large question, and involves many inquiries. For example, is it possible that every cell of ductal epithelium might, under certain circumstances, produce a progeny from which liver-cells eventually proceed, or may it be that just at the point where the diverticulum forms is situated a portion of embryonic bioplasm, which after having lain dormant for many years springs suddenly into activity, and produces many hepatic cells? There is then the further question whether the cells in the diverticulum give origin to secreting and ductal epithelium, or whether the last spreads into the neck of the diverticulum when the latter is connected with a distinct duct.

In some specimens, particularly in the human liver, the ductal epithelium reaches to the point where the true liver-cells commence, Fig. 66, Pl. XX. In certain cases the secreting cells undoubtedly become modified, so as to approach, at least in appearance, the epithelium of the small duct, and notably in cirrhosis, the secreting cells diminish in size, and become harder and more condensed in the marginal portion of the lobule, so as to approach the ductal epithelium in character.

Although the arrangement I have described is very distinct in the liver of the frog and toad, some observers will not allow that the fact can be used as an argument in favour of the view of the anatomy of the mammalian liver, which I contend to be the correct one, because they maintain that what is urged by me in this direction is admitted as regards the structure of the batrachian liver, but in the liver of birds and mammalia according to them exhibits an arrangement totally distinct from that which obtains in fishes and reptilia. However this may be, it seems to me very important to bring before the reader the results of observation upon the liver of various vertebrata prepared in precisely the same manner and examined in the same medium, leaving him to decide whether he will accept the dictum that the liver of fishes, batrachia, and reptilia is constructed according to one, and that of birds and mammalia according to a totally different, type of structure; in fact, that in the one case the tubes containing the secreting cells communicate directly with the efferent ducts, in the other that the cells are surrounded by extremely fine gall-capillaries, which end or commence at different points upon the surface or in the substance of individual cells.

THE DUCTS IN BIRDS.

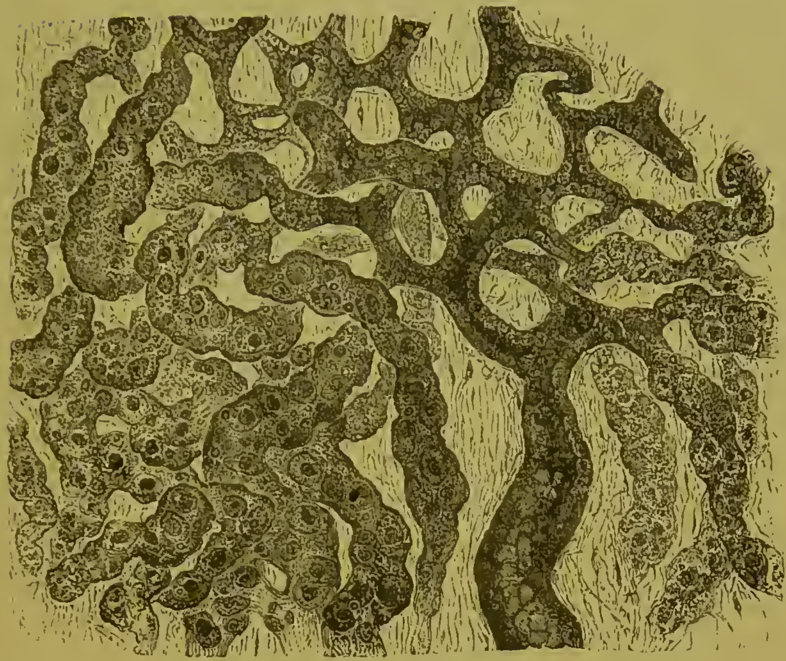
In the turkey, and also in the fowl, I have been able to trace the continuity of the ducts and cell-containing network in injected specimens. The abundance of epithelium in the ducts forms a great obstacle to perfect injection, and the excessive delicacy of the capillaries renders the injection of much water without rupture very difficult. From this cause I failed in many attempts to obtain demonstrative preparations of the arrangement in the bird's liver.

The liver of the bird, though readily obtainable at any period of development, is difficult of investigation during the early stages. Being exceedingly soft and friable at an early period, the study of the changes which occur requires the greatest care. I have in some measure succeeded, by soaking in alcohol and soda the liver of the chick at the fifteenth day, and at the twenty-fifth day, in obtaining fragments showing very clearly the connection between the ducts and the cell-containing network. In Fig. 72, Pl. XXI, the secreting epithelium is undergoing development, and the large tube seen in the drawing would probably give off many diverticula as development proceeded. At this time the elementary parts are imperfectly formed, and have not yet commenced to discharge their function. Neither oil-globules nor biliary particles are yet to be discerned, while in Fig. 73 many oil-globules are to be seen, and probably at this time, the twenty-fifth day, the liver has already begun to perform its function.

FINEST DUCTS AND CELL-CONTAINING NETWORK.

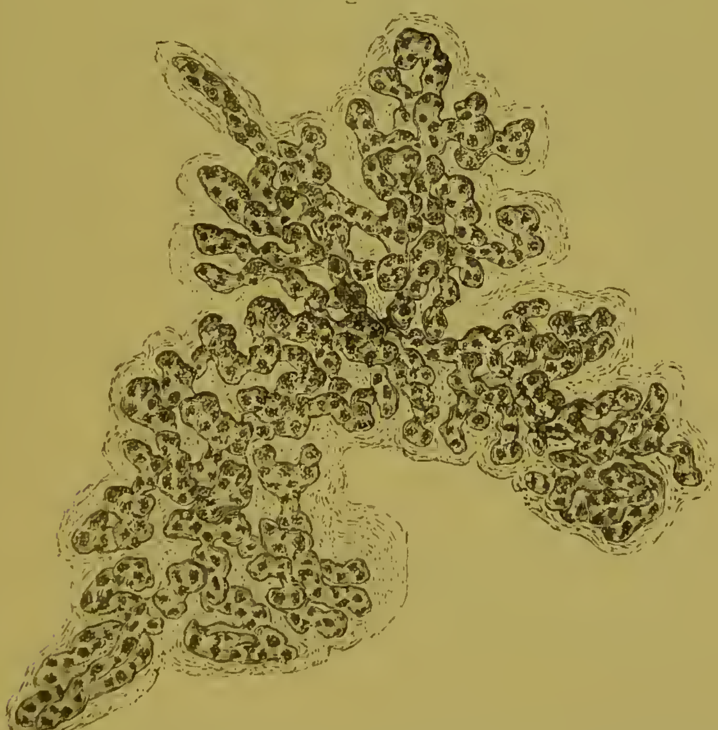
LIVER OF FROG AND TOAD.

Fig. 51.



One of the terminal ducts of the liver of the frog, showing its division into fine branches, which at length expand into the tubes of the cell-containing network. The ductal epithelium is well seen. The regularity of its arrangement round the walls of the ducts contrasts with that of the liver cells, which are irregularly packed in the thin-walled tubes of the network. Injected with Prussian blue fluid. × 120. p. 111.

Fig. 52.



Small separate lobule-like portion of the liver of the toad. One fine duct proceeds from the central part of the network but this is not well seen in the drawing. The manner in which the tubes of the cell-containing network are increased by extension—by offsets from the existing tubes is well seen. × 130. p. 112.

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PLATE XVIII.

DEVELOPMENT OF CELL-CONTAINING NETWORK.

LIVER OF TOAD.

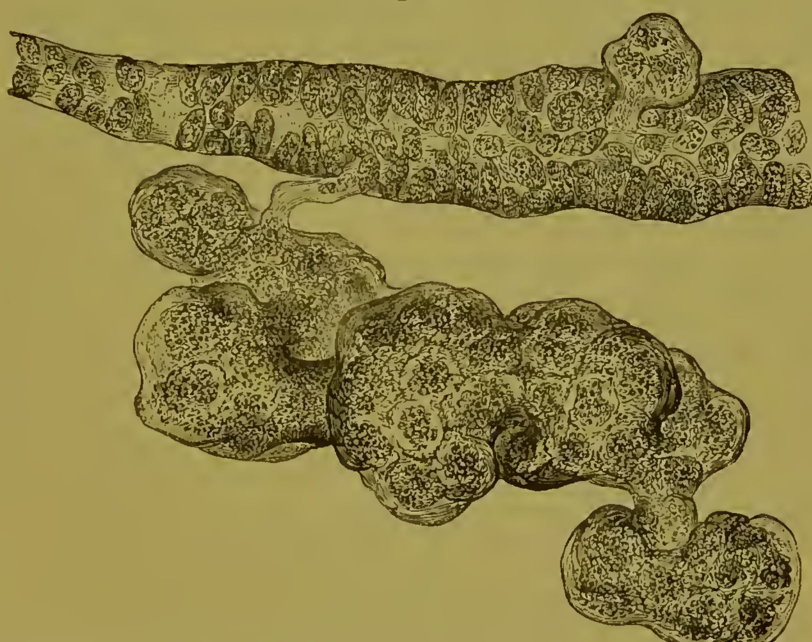
Fig. 53.

Portion of a small duct of the toad's liver, with diverticula containing secreting cells. These are budding and extending so as to form a complex collection as in Fig. 52, Plate XVII. Toad. × 215. p. 112.

Fig. 54.

Duct of liver of toad, with long narrow diverticula containing liver cells × 40. p. 112.

Fig. 55.



A portion of Fig. 53 × 700 diameters. In the upper part of the drawing is a commencing diverticulum which contains liver cells, and there can be no doubt that this springs from the duct; indeed the cells of this part of the duct are modified, and it is difficult to believe that the secreting cells are not ductal cells modified. p. 112.

Fig. 56.

Another small lateral diverticulum from a small duct of the toad's liver, in which the epithelium very closely resembles that of the duct. It is softer and is growing larger. This diverticulum would gradually increase and assume the character represented in Fig. 52, Plate XVII., and Fig. 53 above. × 215.

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DUCTS. CELL-CONTAINING NETWORK.

Fig. 57.

Small duct and its connections with branches of the cell, containing network. *a* The difference between the secreting cells of the cell containing network and the epithelium lining the duct is well seen. Frog's liver. × 350. p. 111.

Fig. 58.

Portion of cell-containing network. Pig, injected. The tube at *a* is somewhat dilated × 215. p. 102.

Fig. 59.

Most superficial portion of the cell-containing network of the lobule of the liver of the pig, lying partly in the fibrous capsule of the lobule, and partly within the capsule. The tubes contain a few small cells, free oil globules, and granular matter. Partially injected with Prussian blue fluid. × 215. p. 102.

Fig. 60.

Cell containing network. pig, within the capsule of the lobule injected with Prussian blue fluid, containing a few secreting cells. × 215. p. 102.

L. [illegible] AD. NAT. DEL., 1851.

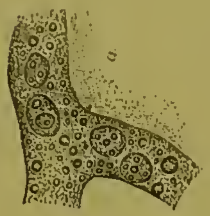
[To follow Plate XVIII.

DUCTS AND CELL-CONTAINING NETWORK.

Fig. 61.

Part of cell-containing network of dog's liver, in caustic soda. Cells fused together. The walls of the tubes very distinct. × 215.

Fig. 62.



Portion of cell-containing network of lophius. × 215. p. 115.

Fig. 63.

A portion of the network on the surface of the lobule of the pig's liver, fully distended with injection × 215.

Fig. 64.

Portion of cell-containing network—lophius. × 215. p. 115.

Fig. 65.

Portion of cell-containing network. Surface of lobule of pig's liver. The cells pressed to the sides of the tubes by the accumulation of injection. × 215. p. 105.

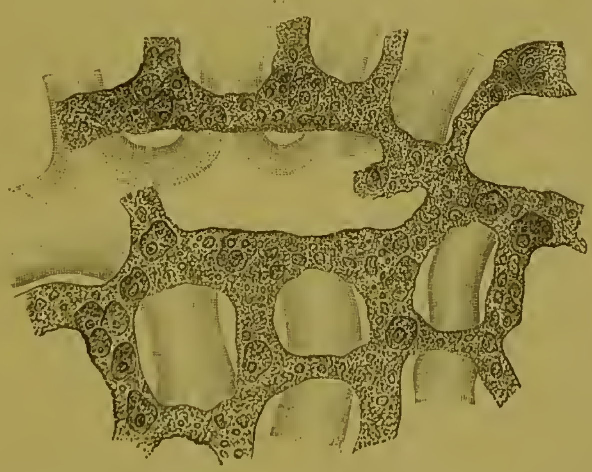
Fig. 66.

Section of hardened human liver, uninjected, showing continuity of ducts and cell-containing network. Hepatic. Cells made transparent by soda. Ductal epithelium very distinct. Specimen has been subjected to great pressure. × 215. p. 104.

Fig. 67.

A part of same specimen as Fig. 66, pressed less severely. × 215. p. 104.

Fig. 68.



Portion of cell-containing network, human fœtus, just where a small branch of the portal vein divides into capillaries. Walls of the capillaries and tubes of the cell-containing network very distinct and separated by an interval occupied by perfectly transparent material. × 215. p. 76.

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DUCTS IN FISHES.

In the investigation of the anatomy of the ducts in the class of fishes, the greatest difficulties present themselves, and very numerous were the failures which I met with in trying to inject them. The difficulty arose partly from the delicate nature of the vessels, which very frequently were torn in attempting to inject them with water, and partly from the soft, pulpy, and exceedingly fatty condition of most of the livers of animals of this class.

In the sturgeon the connection is shown in Pl. XXI, Fig. 69, *b*, *c*, and *e*. The secreting tubes represented are smaller than is usual in this class, depending upon exosmose of their fluid contents. The shrinking thus caused enables us to distinguish the outline of the tubes very clearly. I have also succeeded in injecting the ducts of the flounder and frog-fish (*Lophius piscatorius*); and the connection between the very narrow ducts and the cell network of the latter is represented in Fig. 70, Pl. XXI, p. 116, and the tubes of the network in Figs. 62, 64, Pl. XX.

Even in the fatty liver of the cod I once traced the continuity between the narrow ducts and the very wide tubular network distended with cells containing oil and free oil-globules.

In injecting the livers of fish, the injection must be diluted with weak spirit, or it does not penetrate to the smallest branches. The colouring matter which is employed is the same as in other cases. Often the particles of the injection accumulate in some of the finer ducts, forming what appears to be rounded and slightly dilated extremities; for the further continuity of the tube cannot be detected. Indeed, so perfect is the resemblance, that it is only by carefully examining many different specimens that the fallacy is detected.

General Conclusions regarding the Ducts.—In all the vertebrata, the arrangements of the ducts, and the relation which they bear to the secreting cells, is very similar. I have seen both in injected, and also in uninjected, specimens the communications between the finest ducts and the cell-containing network. Of the nature of this continuity there can, I think, be no doubt. I can conceive no other explanation of the facts I have observed, or of the appearances presented by my preparations. The observations upon uninjected specimens, shown in Pl. XX, Figs. 66 and 67, were made early in 1854, some months before I had succeeded in injecting the ducts. The arrangement of the most minute ducts near the cell-containing network varies somewhat in different animals, as has been described. In some they form a network of very narrow tubes, continuous with those in which the liver-cells are contained; in others, the communications are excessively few in number, and the fine ducts are completely destitute of any cells,

or contain only a very few rounded cells less than a red blood corpuscle. The fine duct suddenly dilates or becomes the comparatively wide tube containing the secreting cells, there being no communication or anastomoses between the ducts.

The liver-cells correspond in all essential particulars to the secreting cells of other glandular organs. They lie within a cavity of thin delicate membrane, which is here arranged so as to form a network, the tubes of which are directly continuous at various points with very narrow efferent ducts. This narrowing of the duct before it becomes connected with the *secreting* portion of the organ is seen in other glands. In the kidney, the total diameter of the straight and ductal portion of the renal tube is considerably less than that of the convoluted and glandular part, although the central cavity is wider, which allows of the very rapid removal of the secreted products formed in the convoluted portion of the tube. Small as it is, the cavity of the very narrow ducts of the liver would doubtless admit the passage of a larger quantity of fluid, within a certain time, than the variable and irregular interstices existing between the cells and the basement membrane in the secreting portions of the network. In the liver, where the secretion is highly elaborated, and slowly removed from the secreting structure in a comparatively concentrated form, we should naturally expect to find the contrast between these two different portions of the gland. Moreover it must be borne in mind that the bile is a fluid which has special properties of passing through the most minute channels. If distilled water has a very small quantity of glycocholate and taurocholate of soda dissolved in it, it will "wet" almost anything, and run into the smallest interstices.

Epithelium of the Smaller Ducts.—The larger bile ducts, as is well known, have a thick lining of well-developed columnar epithelium; but the cells become shorter as the smaller channels are reached. In the smallest ducts, the cells of epithelium are somewhat flattened, and are of a circular or oval form. The latter appearance, at least in some instances, seems to be due to the ducts being much stretched in preparing the specimen. These minute cells have a pale granular appearance, and it is not often that a nucleus can be distinctly seen within them. The epithelium of the ducts is not dissolved by caustic soda so readily as the liver-cells; indeed, the former cells are scarcely altered by weak solutions, while the latter are rendered very soft and transparent. The quantity of this epithelium in the smaller ducts varies very much; sometimes it completely lines the tubes; in some instances it is so abundant as apparently to leave no distinct cavity in the duct (a condition I have met with in the rabbit, turkey, and fowl): while it is not uncommon to find some of the finest ducts, containing only a very few cells, scattered at irregular intervals over the very thin membrane, of which the walls of the small ducts are entirely composed. In a

PLATE XXI.

LIVER OF FISH, NEWT, AND BIRD.

Fig. 69.

Branching of the ducts and their connection with the tubes of the cell containing network of the sturgeon. *a*. duct distended. *b*. tubes of cell containing network. × 42. p. 115.

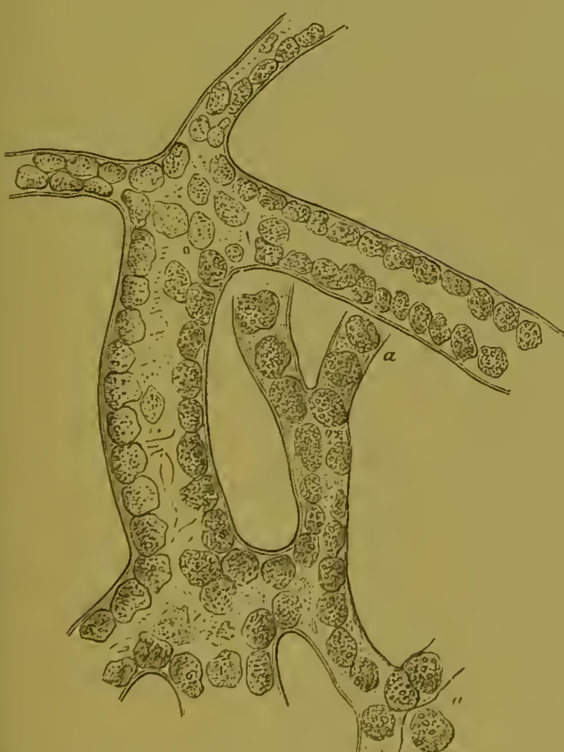
Fig. 70.

Finest ducts of lophius piscatories and connection with cell containing network. × 215. p 115

Fig. 72.

Part of cell containing network and finest ducts of chick on the 15th day of incubation, from a preparation which had been hardened in alcohol and soda × 215. p. 114.

Fig. 71.



Branches of duct of newt (triton cristratus). The commencement of the tubes of the cell containing network is well seen at *a*. *a*. × 215. p. 111.

Fig. 73.

Tubes of cell containing network of chick on the 21st day of incubation. The liver cells now contain oil globules. × 215. p 114.

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perfectly normal condition, when the minute ducts are undisturbed by manipulation, and are examined in a proper medium, they are generally seen to be lined by epithelium; but, from the extreme minuteness of these ducts, and the tenuity of their walls, and not less from the very delicate nature of the epithelium itself, there is no wonder that we should fail in making out distinctly their epithelium in every instance in which we search for it.

It is not easy to lay down with precision the exact point at which the change in the character of the epithelium of the ducts occurs; but it appears to me that at least in some cases the alteration is a gradual one, and that the cells become shorter and shorter as the diameter of the ducts diminishes. In ducts of the 1-600th of an inch, and in smaller ones, the epithelium presents the characters above described. This ductal epithelium does not as a rule pass by insensible gradations into the secreting epithelium, or hepatic cells, but ceases abruptly at the point where the narrow duct becomes continuous with the wide secreting cell-containing network.

When the ducts are injected, according to the method described in this volume, the epithelium and the injection may be seen very distinctly with a quarter of an inch object-glass, in narrow tubes, often not more than the 1-3000th of an inch in diameter.

Diameter of the Finest Ducts.—The diameter of the finest ducts can only be obtained approximately; for, when not injected, they can only be demonstrated distinctly in fortunate specimens, and are probably somewhat narrower than during life. When injected, on the other hand, they are usually distended, and sometimes to a very considerable extent. In the pig, the smallest branches containing a little injection are not more than the 1-3000th of an inch in diameter; in the human subject, about 1-2500th; in the seal, 1-3000th; in some fishes, not more than 1-5000th.

The diameter of the cavity of the tube and total diameter of ducts of different sizes are shown in the following Table:—

	External diameter.	Diameter of channel.
Pig	·008	·004
	·006	·003
	·001	·001
Human subject ...	·01	·0045
	·002	·002
Human fœtus... ...	·01	·0045
Cat	·015	·0075
Monkey	·02	·01
Seal	·001	·001
	·0003	·000

GENERAL CONCLUSIONS CONCERNING THE VERTEBRATE LIVER. THE VERTEBRATE AND INVERTEBRATE LIVER COMPARED. THE LIVER AND KIDNEY COMPARED. POSITION OF THE LIVER AS A SECRETING ORGAN. SUMMARY.

The Vertebrate Liver.—The vertebrate liver may be looked upon as consisting essentially of two distinct systems of tubes arranged so as to form *solid** networks which mutually interlace with one another. In one of these networks lie the secreting cells, often arranged so as to form only a single row, which is, therefore, surrounded by the blood containing the elements from which the bile is to be formed. The fluid bile escaping from the cells into the membranous tubes flows towards the surface of the lobule where the ducts lie. In the other network flows the blood, but in a precisely opposite direction to that which the bile takes.

The *portal blood* reaches the capillaries of the lobule at many different spots upon its surface, and all the blood from the numerous venous branches passes through capillary vessels which converge towards the single radicle of the hepatic vein in the centre of the lobules. Hence it follows that the circulation of the blood must be much more rapid in the central part of the lobule than near its portal surface. This harmonizes with many anatomical facts which I have already alluded to. The blood which has just arrived from the intestines, laden with recently absorbed constituents, flows very slowly, in order that the liver-cells may have time to act upon it, and remove from it certain constituents. When the greater proportion of these have been separated, the slow course of the blood is no longer of advantage, and, as the circulating blood becomes purer, it flows with increasing velocity, until the streams having converged towards the centre of the lobule, the blood is at last poured into the large inferior cava.

By the very simple and beautiful arrangement of the elementary tissues of the liver, so as to form minute portions resembling each other, or *lobules*, the most complete change in the mass of the portal blood is ensured, while the circulation is retarded in the least possible degree compatible with the alteration to be produced. At the same time the anatomical elements, instrumental directly in effecting these changes, are combined in such a manner as to occupy the smallest possible amount of space, consistent with free action.

The cells in all parts of the network have, no doubt, the power of forming bile, but in different degrees. Even those quite close to the centre of the lobule have occasionally been observed to contain yellow granules. The cells at the circumference of the lobule secrete very

* This term was, I think, first employed by Sir William Bowman, *vide* article "Mucous Membrane," Todd's Cyclopædia of Anatomy and Physiology.

actively, and those near the centre of the lobule very slightly or scarcely at all. It is probable that the elementary parts actually in the centre in health, and more especially during the early period of life, are growing and multiplying rather than producing secretion.

In the elaboration of the bile there is no reason for supposing that the secretion is passed from cell to cell, and at last into the duct. If this were the case, we should expect to find greater difference in the cells near the ducts than really exists; and it must be remembered that in many animals in a state of perfect health no difference whatever is to be demonstrated. It is to be remarked that the cells at the circumference of the lobules of the human liver usually contain a much larger quantity of oil than those nearer the centre. This is exactly what we should anticipate when we consider that the portal blood, rich with the freshly absorbed constituents of the food, first reaches these marginal cells. The direction of the circulation is the reverse of that which we should expect to find if the secretion were transmitted from cell to cell, most active work being carried on at the surface of the lobules nearest to the portal canals and interlobular fissures. The anatomy of the organ almost forces upon us the conclusion, that the cells nearest to the duct take the most active part in the secretion, and that the blood gets depurated and is gradually rendered more free of substances from which the bile is formed, while travelling along the capillary tubes from circumference to centre, with a gradually increasing rapidity of movement. Lastly, the assumed absence of any channel in which bile could flow is not tenable, because it has been shown to be comparatively easy, provided that certain precautions be observed in conducting the operation, to force injection into a channel which does exist. It may fairly be argued that if, by artificial means, fluid can be made to pass in an opposite direction, within the tubes of this cell-containing network, up to the hepatic vein, it is certain that a channel must exist along which the bile, a fluid remarkable for its properties of flowing through the smallest channels, will readily pass during life, and be delivered to the duct as fast as it is produced.

This large and important organ presents us with an example of gland structure in which the different tissues of which it is composed are arranged in the most advantageous manner it is possible to conceive. The secerning cells and the blood are brought into the closest proximity possible. The blood containing the crude elements is separated from the cells whose office it is to elaborate these constituents, only by the intervention of the thin capillary walls and a membranous partition, under ordinary circumstances not visible, and so delicate that its existenee is disputed by many great authorities. The areolar tissue, which serves to support the capillaries of most glands, is here absent, and the wall of the capillary comes into close

contact, and in many instances is incorporated, with the thin transparent membranous tube in which the liver-cells lie.

The alteration in volume which the cells may be made to undergo by artificial means indicates how very simply a channel may be produced if the cells shrink a little in volume. The two sets of tubes, blood-containing and cell-containing, mutually adapt themselves to each other; and if the secreting tubes be unusually empty the vascular tubes admit more blood. It has been already pointed out what a very large proportion of fluid the capillary vessels of the liver are capable of containing over and above what may be assumed to be their normal quantity, and also how the distension of the vessels, by forcing fluid in one direction, promotes the passage of liquid through the cell-containing network in the opposite direction. Careful reflection upon some of these circumstances assists much in the comprehension of many of the morbid changes which take place in the liver.

The bile having arrived at the smallest ducts, without doubt undergoes further changes. It is not improbable that the oxygen brought by the arterial blood which flows in the vascular network, through the meshes of which the ducts pass, exerts some influence upon it. This, however, has not been proved. The most important alteration which the bile now undergoes is concentration. Water is removed, and the proportion of solid constituents gradually increases as the bile passes slowly along the thin-walled, tortuous ducts. It is this change which serves to explain the comparatively slight increase of diameter of the ducts, in proportion to the great number of branches which they receive. Thus the apparent disproportion between the vast amount of secreting structure and the small efferent ducts vanishes, when we consider how highly concentrated the bile becomes before it reaches the large duct. Bile contains a larger proportion of soluble constituents than any other liquid secretion.

The manner in which this concentration is effected has been alluded to. In those animals provided with a gall-bladder, it has been shown experimentally by Bidder and Schmidt that much fluid is absorbed while the bile remains within this viscus. It is interesting to observe that the arrangement of vessels and lymphatics in the portal canals and transverse fissure of the liver is very similar to that which is met with in the gall-bladder. The bile is brought into very close relation with the vessels, by entering the little cavities, *parietal sacculi*, in the coats of the ducts and in the vasa aberrantia, which are always surrounded by numerous branches of the vein and artery, and by lymphatic vessels.

In some instances the inspissation of the bile is carried to an abnormal extent, and small, tolerably hard granules of biliary matter are eventually produced. These often form the nuclei of gall-stones,

and sometimes accumulate in great numbers in a branch of the duct. Although a calculus might become impacted in a duct, the free transmission of the bile is fully provided for by the numerous anastomosing branches, just external to the duct itself, which have been described in p. 49. *See* Pl. V, Figs. 11, 12, 13, 14, Pl. VII, Figs. 20, 21, 22.

The Vertebrate and Invertebrate Liver compared.—It has been said by many writers that there is a great difference of structure between the livers of the vertebrata and the invertebrata; but the more carefully the vertebrate liver is examined in its minute details, the more convincing will appear the evidence that both resemble each other in many essential particulars. Nay, in some of the lowest of the invertebrata, the general minute anatomy of the liver closely accords with that of the organ in the highest animals. In the large intestine of the common frog, a small entozoon of the trematode order is very often met with. In some of these, which were taken from the body of a starved frog, the biliary follicles and their ducts were very distinct. The cells in the follicles contained colouring matter, and but very little oil. The follicles, being somewhat shrunken, could be examined very satisfactorily. The follicle terminates in a cæcal extremity, but is prolonged at the opposite end into a very narrow duct, which is soon joined by the ducts from other follicles. Suppose the cæcal extremities extended, and communicating with each other, so as to form a network, and an appearance closely resembling the drawing of the connection between the ducts and cell-containing network in Fig. 52, Pl. XVII, p. 114, would result. The cells appear to contain colouring matter and oil, either in a granular state or in the form of distinct globules, in all classes of animals; they exhibit the same general character, and they lie in the tube or follicle without order or regularity, their form being influenced to a considerable extent by mutual pressure. It is impossible to help seeing a similarity in the arrangement of the cæcal follicles, with their narrow necks, around some of the ducts of the higher animals, and a comparison between this and the follicular condition of the entire organ in many of the mollusca and crustacea may fairly be made.

In the different members of the animal creation, the liver-cell seems to preserve certain constant peculiarities; and in the development of the young animal, the cell soon attains the character which it bears throughout life, except that at this early period it contains a greater number of nuclei. This comparison is exceedingly interesting, and points to the great similarity in essential arrangement, and, in fact, to the existence of a common type as regards the liver in animals occupying very opposite positions in the animal scale.

The Liver and Kidney compared.—The bile and the urine, the two most important secretions in the body, have often been contrasted, and

their opposite or complementary nature has been pointed out. It is interesting to compare the anatomy of the glands which secrete these dissimilar fluids.

The *kidney* is an organ destined for the rapid removal of substances largely diluted with water, the most important of which, at least, exist pre-formed in the blood. A tortuous tube of delicate membrane, closed at one end, lined in its interior with cells, but having a free central cavity, is the essential apparatus by which this is effected. At the closed extremity of the tube is a special provision for the separation of water, which, as it passes down the central cavity, readily dissolves away the soluble matters which the cells have separated and elaborated from the blood. The solution quickly passes down the tube, and, without undergoing further change, is soon removed altogether. So important is the rapid removal of the urinary constituents from the organism, that in some animals in which a sufficient quantity of water for the complete solution of the excrementitious matters cannot be afforded, there exists a most perfect and beautiful arrangement by which the desired thorough removal from the system is attained, but in a totally different manner. Not only is there a cavity throughout the entire length of the tube, but the cells around it are furnished with vibratile cilia, by the action of which even solid particles are whirled down the tube with a velocity greater than that of the circulation of the blood in the capillaries.

In the *liver*, on the other hand, we have an organ not only for the separation of substances very recently taken up from the intestine and introduced into the organism from the portal blood, but for the slow elaboration and conversion of these into very different products which serve important ulterior purposes in the economy, and which are in great part re-absorbed into the blood, while at the same time it is probable that a change occurs in other constituents of the blood as it traverses the capillaries of the liver. A network of delicate tubes, almost surrounded by blood flowing through capillaries, containing large secreting cells in their interior, arranged irregularly and nearly filling the cavity, leaving only here and there irregular and very narrow channels for the passage of the secretion, is the essential apparatus for the formation of the proper secretion of the liver. The secretion, when formed, may remain for some time in the tubes, but will slowly make its way in an opposite direction to that in which the blood flows, through narrow channels, between the cells or between these and the walls of the tube, until it arrives at the narrow efferent duct. Still passing slowly along these delicate tubes, it becomes exposed to the influence of arterial blood, while much of its water, probably holding in solution substances capable of permeating the basement membrane in this direction, is re-absorbed by the veins and lymphatics, which form an

intimate plexus round the ducts. It has been shown how effectual is the provision for the concentration of the bile throughout every part of the ducts from the point where they commence as very narrow tubes to their termination in the common gall duct. Unlike the urine, the bile undergoes important alterations after it has been set free by the cells, in its course along the ducts, and it is probable that but a small proportion of the total quantity formed in the liver is entirely removed from the organism without previously undergoing many other changes.

Position of the Liver as a Secreting Organ.—The liver, then, should, I think, be classed with the true glands, and in vertebrata it is the largest, perhaps the most important, of them all. In all classes of animals it consists of a *formative portion* and of an *efferent duct*, the epithelium in these two situations presenting characteristic differences. It contains absolutely and relatively a greater proportion of true secreting structure than any other organ. Its secretion is of the most complex chemical composition, and perhaps differs more widely from any known constituents of the blood than any other secreted product. The liver serves a great number of important purposes in the economy, and it is probable that we have yet much to learn concerning its work. The amount of bile separated by the liver in twenty-four hours is far larger than that of any other liquid secretion, from a single gland or organ, and at the same time it contains a higher percentage of solid matter.

The early appearance of the liver, its large size both in the embryo and in the adult, its almost universal presence and general similarity of structure in all classes of animals, the chemically complex nature, the large quantity and highly concentrated state of its secretion, justify us in regarding the liver as the most important gland in the body. The size and vast number of its cells, their close proximity to the blood, and the beautiful arrangement of the other anatomical elements of which it is composed, render it, I think, the most perfect example of gland structure with which we are acquainted.

SUMMARY.

The livers of all vertebrate animals are penetrated in every part by two sets of channels, which alternate with each other. One series, *portal canals*, contains a branch of the portal vein, hepatic artery, and hepatic duct, *interlobular;* and the other series, *hepatic venous canals*, is occupied by a single branch of the hepatic vein, *intralobular*.

Division of the Organ into Lobules.—The vessels and ducts ramifying in the portal canals are ultimately distributed in such a manner that they serve to divide the organ into little masses, and thus

map out portions of hepatic tissue, or *lobules*, each of which contains all the structural elements of the organ, and is to be regarded as a complete *elementary liver*. A small liver contains comparatively few lobules; in a large liver the lobules are very numerous.

In the intervals between the fissures by which the portal vein, artery, and duct are conducted to the lobule, the capillary vessels and the secreting structure of the lobule are continuous with those of adjacent lobules.

The size and form of the lobules differ much in different animals; but their essential structure is the same in all, except in the pig, in the Polar bear, according to Müller, and in the *Octodon Cummingii* (one of the rodents), according to Hyrtl.

In these exceptional cases the liver is divided into a number of distinct and separate lobules, each provided with a capsule of its own, just as the kidney of the porpoise and of the seal is divided into a number of separate renules.

In the *pig* then each lobule is provided with a separate fibrous capsule of its own, and is, therefore, completely isolated from its neighbours. Branches of the portal vein, artery, and duct run between them, and give off branches to contiguous lobules. In the intervals between the fibrous capsules areolar tissue can frequently be demonstrated.

In all cases, upon section, the lobule is seen to be bounded externally by branches of the vein, artery, and duct, and in the centre is situated a small branch of the hepatic vein.

Areolar Tissue in Portal Canals.—In the liver of the human subject, and in that of vertebrate animals generally, with the exceptions above mentioned, the lobules are not separated from each other by any fibrous partition, and there is no areolar or fibrous tissue, or extension of "Glisson's capsule" between them, or in their interior.

The vessels at their entrance into the liver, and as they run for some distance in the larger portal canals, are surrounded with much areolar tissue; but the disposition of this texture about the vessels of the liver is very similar to its arrangement about the larger vessels distributed to other organs.

Intimate Structure of the Lobule.—The *lobule* itself is composed of a solid capillary network, and of another network composed of a very delicate tubular membrane, in which the liver-cells are contained.

These networks mutually intertwine with each other.

The capillary network is directly continuous with the smallest *interlobular* branches of the portal vein, distributed upon the circumference of the lobule on the one hand, and with the small *intralobular* branch of the hepatic vein arising in its centre upon the other. The vessels of the network converge towards the centre of the lobule.

Small branches of the *artery* open into the venous capillaries of the lobule, near its circumference, and the diameter of these small branches is considerably less than that of the venous capillaries into which they open; the former not more than the 1-4000th of an inch in diameter, the latter about the 1-1600th.

In all cases, the blood, enriched with constituents recently absorbed from the intestine, flows with a gradually increasing rapidity from the circumference of the lobule towards its centre, while the bile flows in a precisely opposite direction.

Of the Liver-cells and of the Tubular Network in which they lie.— The liver-cells lie within a tubular network of basement membrane, which separates them from the walls of the capillaries. In many cases, however, these thin membranous tubes cannot be separated, and are, no doubt, incorporated with one another.

The cells are not attached to the basement membrane of the tube, but lie in its cavity. Among them free oil-globules and granular matter are often found. Usually, there is room for only one row of cells, but sometimes two or more lie across the tube. In the embryos of mammalia, in young animals generally, and in fishes, there is room for several rows to lie transversely across the tubes of the cell-containing network.

The cells near the margin of the lobule take the most active part in the formation of bile. The secretion passes along the tubes in the slight interstices between the cells and the basement membrane, and coloured fluid can be forced along these same interstices in a direction the opposite to that in which the bile flows during life, and, therefore, at a great disadvantage. The amount of space is in great measure determined by the quantity of blood in the vessels, and it is liable to great alteration.

The cell-containing network is directly continuous with the most minute ducts, which ramify at the circumference of the lobule, and it terminates in the centre by loops, which lie close to the intra-lobular vein.

Of the Finest Ducts.—The tubes of the cell-containing network are many times wider than the narrow thin-walled ducts with which they are directly continuous.

The smallest *ducts* contain delicate epithelium-like cells, some of which are *flattened*, of a circular form, contrasting remarkably with the large *secreting cells*, which are not arranged in any definite manner within the tubes of the network.

The tubes of the cell-containing network are about 1-1000th of an inch in diameter, or more, but the finest ducts are commonly not more than 1-3000th, and they are often seen much less.

The smallest ducts in some animals branch very freely, and the

branches communicate with each other at intervals. In others they pursue a long course without branching, and in the pig they form an intimate network upon the surface of the lobule. In fatty livers of the pig, however, this ductal network often contains liver-cells loaded with oil-globules.

As the ducts increase in size they are provided with a fibrous coat, and the epithelium in their interior becomes columnar.

Interlobular ducts on reaching the lobule from different points do not anastomose.

Sacculi in the Coats of the Ducts.—When the fibrous coat reaches a certain degree of thickness it contains numerous little cavities, or *sacculi*, arranged entirely round the tube in the pig and in most animals, but forming two parallel rows, one on either side of the duct, in the human subject.

These little sacculi often communicate with each other in the coats of the duct. The smaller branches of the duct also anastomose frequently, either in the coats of the duct or just external to them.

The sacculi appear to serve the purpose of bringing the bile in the thick-walled ducts into closer relation with the vessels which surround them, and especially with the branches of the artery which are distributed to their coats.

Vasa Aberrantia, and of the Arrangement of the Vessels around them.—In the transverse fissure of the human liver and of some others, are found in the large portal canals some peculiar branches of the duct, *vasa aberrantia*, with numerous sacculi on their walls. These branches anastomose with one another and form a network.

In the same localities in the human subject, and in the gall-bladder, a very peculiar arrangement of the vessels occurs. Both arteries and veins form a network, and each branch of the artery is accompanied with two branches of the vein, one on either side of it.

DERANGEMENTS OF THE LIVER FOLLOWED BY A RETURN TO THE HEALTHY CONDITION, OR RESULTING IN STRUCTURAL CHANGE.

The proper action of the liver, both as regards bile formation and the production of other substances which are returned to the blood where further changes are effected, is necessary for the health, not only of the liver itself, but of all the tissues and organs of the body. Hepatic action has much to do with the activity and regulation of complex processes connected with blood distribution and the nutrition of the different tissues and organs, and there is no doubt that it exerts a very important influence upon the highest of all the organic phenomena, mental action. Not only is the nutrition and action of the brain and nervous system dependent upon a healthy condition of liver, but it is doubtful whether the development of these, the most important textures in nature, could proceed if the liver had not been previously in a healthy, active state, so that the special substances it was to elaborate for direct or indirect influence should be produced.

The liver being very intimately concerned in rendering equable and regular the work of the body in health, is necessarily very sensitive to changes, and is easily deranged, while the rate of its action is liable to frequent and considerable variation. It will nevertheless submit to very decided ill usage without deteriorating in structure, and after even prolonged derangement it will probably soon return to its normal state. If, however, the disturbance to which it is subjected persists, the organ may suffer permanently, and undergo very decided change in structure. It may afterwards degenerate and waste long before old age is reached, when such pathological alterations slowly occur in the ordinary course of things.

In the most healthy great modification in the activity of the liver is frequent. It may pass from a state almost of quiescence to one of considerable activity, and in a very short period of time. By frequent vacillation in hepatic activity, steadiness and uniformity of action as regards other processes is established. Tendency to variation in the composition of certain chemical substances is probably checked, or, if it has occurred, compensated for by hepatic action; and especially in cases where the body is exposed to considerable changes of temperature, is variation of the body heat in health guarded against.

The liver-cell is the agent which, by the varying rate of action, contributes to the production of the uniformity of the body heat, which is preserved notwithstanding continual variation in temperature of the surrounding medium. The liver-cell may thus be said to preserve

uniformity, not only, I think, as regards body heat, but by preventing or compensating disturbances which necessarily result from tissue action.

Frequently in infancy and childhood does the action of the liver become sluggish, or it may be almost suspended for days together, and in adult life and in old age such disturbance is not infrequent. The motions are at these times pale and scanty, of a clayey consistence, and offensive smell. The patient's general health is disturbed, there is lassitude, sensation of being tired, perhaps with aching of the limbs, loss of appetite, a sensation of nausea, more or less headache, and the feeling as if the patient had "taken cold." There is indisposition to eat, inability to think or to fix the attention for any length of time; the intellect becomes cloudy, thought is confused, the memory is temporarily impaired; giddiness, and perhaps an actual tendency to fall, is experienced, and probably these symptoms cause alarm both to the patient and his friends.

It is very remarkable for how long a time the action of the liver may be almost suspended, and it is not uncommon to meet with individuals who suffer in this way for two or three weeks at a time. At some periods of life this hypersensitiveness of the liver seems to be more frequently present than its normal action, and the greatest care has to be continually exercised as to diet. At these times very little food should be taken. The organ requires rest until it resumes its normal action, when the patient may eat again as usual. While he suffers he should eat very little meat, and should depend for sustenance upon milk and farinaceous food, easily digested vegetables, and fruit, particularly bananas, if these can be obtained. It is to be remarked that of those who thus suffer many are naturally small eaters, or become so. Possibly this is the explanation of the longevity of many such persons, and of their escape from serious illness. Some of them seldom or never feel really well, although perhaps they have never been attacked by any serious illness. This highly sensitive condition of liver, while it protects from morbid changes, is scarcely a condition to be desired, for it may almost prevent a man from following some pursuits, and certainly from engaging in many of the amusements and social enjoyments of the majority. Without free action of the liver no one, at any rate without much suffering, can conform to the feeding customs of good society.

When the action of the liver is disturbed in the manner indicated, it will be often found that relief will be afforded if the quantity of liquid taken during the twenty-four hours be considerably increased. From a pint to two pints of aerated distilled water may be recommended, half a tumbler at a time, at intervals. Noxious matters which have accumulated in the tissues are in this way washed out, and an abundant flow of urine will be followed by the much desired relief. On the other hand, if during such a state of inaction of the liver the usual quantity,

or more than the usual quantity, of food (especially of meat) be taken, the digestive organs become gorged with blood, and their action greatly disturbed. If relief is not quickly afforded by vomiting or purging, excrementitious substances accumulate in the blood, and the illness thus occasioned may lay the patient up for some time. Exposure to cold, accidental shock, or over-fatigue may cause congestion of lungs or other internal organs, followed by serious, and possibly extensive, inflammation, which may endanger life, or set up chronic disease.

Although the quantity of food introduced into the body in a given time varies greatly, and the effects of the irregularity are enhanced by the variation in external temperature, by the amount of exercise, and the varying action of the muscular and nervous tissues, the equable distribution of nutrient matter, like the body temperature, as already suggested, is ensured by the variation in the quantity of excrementitious matter removed, and in these processes the liver is specially concerned. If the liver is not in a healthy condition the varying action of certain tissues and organs soon results in serious derangement, and especially in the development of a febrile state of system, from which the return to the normal condition can only be brought about by slow degrees.

The action of the liver, like that of other glandular organs, is greatly, and sometimes almost suddenly, influenced by changes occurring in the nervous system. During the early period of life, and in healthy adults, the influence of change in the nerve-centres is very decided. Emotional excitement seems to exert a direct and almost immediate action. In some cases the individual is at once aware of hepatic disturbance, and sometimes of the almost sudden suspension of the normal changes. There is a sensation of fulness in the hepatic region, with slight nausea and indisposition to take food, and in many cases, if not actual headache, at least an uncomfortable slight aching over the brow and vertex, with sluggish and disturbed intellectual action, and an exceptional slowness of reception and expression of ideas, and for the time impaired memory.

The intimate relation between hepatic and intellectual action has been recognised from the earliest times, and many individuals only too frequently experience in their own organisms the dependence of the activity of the mind upon the proper action of the liver. It is probable that for the highest attainable action of any particular brain, its owner is very dependent upon the proper action of his liver, while there is good reason to think that the varying quality of mental work is in great measure due to fluctuations in the activity and other temporary vacillations of hepatic function; nay, it is very probable that the nutrition of all parts of the nervous system, and particularly of the brain, is very intimately related to free and proper action of this important organ. The action of liver during school life and early manhood is of the

utmost consequence, and may have much to do with success in these examination days.

But while there can be no question that imperfect action and occasional inaction of the bile-preparing action of the liver are productive in some cases of serious disturbance of the health, and inconvenience and discomfort to the patient, it is quite certain that the effects resulting therefrom are not of a nature to cause early tissue deterioration, or to interfere with longevity. It is well known that an individual with a weak and highly sensitive liver and digestive apparatus, often not only outlives, but exceeds in working capacity and enduring power, many who have been stronger and more vigorous in these respects from birth. Those who feel strong and enjoy free and vigorous organ action are sometimes encouraged to overtax their powers. An undue amount of work, perhaps, leads to strain, followed by weakness not to be repaired, and too great reliance upon unusual strength and vigour may result in premature degeneration in, and damage of, important tissues, and, perhaps, early death.

As age advances, the liver, like many other organs, becomes less sensitive to nerve changes, and in old age weeks or months may pass without any derangement, although at an early period of life normal hepatic action was the exception. In some individuals it is true this troublesome over-sensitiveness seems altogether absent. The liver may in consequence become highly congested, and its delicate structure may even be damaged without its owner being aware of the fact. In such persons hepatic disturbance may proceed, and structural changes of the most serious kind be induced, without any symptoms, or even discomfort, being caused. I have known many cases in which the liver had much increased in volume, and cirrhotic change had far advanced, without the patient having suffered in the slightest degree. Indeed, violent and dangerous hæmorrhage, consequent upon structural changes which had been going on for four or five years, or even longer, has been the first indication to warn the patient that anything was going wrong.

Although there is, perhaps, no question connected with derangement of the health upon which so much has been written or so much advice given as on functional disturbance of the liver, we are still but imperfectly acquainted with the exact nature of the changes which actually take place, or with the initiatory phenomena that determine hepatic disturbance. The subject is a most difficult one to investigate, and, whatever may be the exact nature of the disturbance, it is almost invariably associated with so much derangement of other organs, that when we come to study the matter from the clinical side, it is not possible to indicate precisely the symptoms which are due to the liver and those which depend upon the associated stomach and bowel disturbance, and

to the still wider and more general derangement of the nervous system, so very closely, and in some cases causally connected with the digestive and hepatic derangement.

No wonder then that the sufferers from functional liver-derangement are assured by some authorities that the liver is the peccant organ, and by others that the stomach is wrong, by others again that the large or small bowel is at fault, and by not a few eminent advisers that the trouble is all in the nervous system, and the last are careful to emphasize their view by pointing out that nerve-tissue is co-extensive with all the organs, and is the source of all action, the impressionable recipient, the register and corrector of every disturbance of nutritive equilibrium —a conclusion which, however, is only in part true, and by no means approaches a correct estimate of the facts. The claim indeed rests upon a very imperfect consideration of the facts; it would perhaps be nearer the truth to say that the healthy action of the nervous system depends upon that of the liver. Indeed I think, as our knowledge advances, we shall have to restore to the liver that pre-eminence in ensuring healthy functional activity, and in bringing about disturbance of health in respect of I might almost say the whole system, which it held in the time of the ancients, and perhaps still holds in the minds of many thoughtful and practical men.

The healthy liver is so easily deranged in its action that the slightest departure from the normal condition in a number of very different ways will affect it. Complete rest for some hours will, if the derangement has not been kept up for too long a time, and has not gone too far, enable it to right itself, and as it were of itself restore healthy action. Even after the liver has been persistently subjected to increased action for a considerable period of time, it will return to its normal action if only it is allowed to rest, but the arbitrary views of some advisers, and the obstinate prejudices of the sufferers, too often interfere, and the organ is not allowed to get right.

In considering the real nature of an early departure from the healthy condition in the case of an organ so complex in its structure as the liver, we must endeavour to ascertain precisely where—in what particular tissue or fluid—the change in question begins. It is obvious that the departure from the normal condition may begin in the cells which separate certain matters from the blood, in the vessels, or in the blood itself. If we are satisfied that the first change occurs in the matter of the cells, we must try to ascertain whether the nucleus or living matter (bioplasm), or the matter on the surface of the cell (formed material), is first affected. And when we find the cells over the whole lobule are altered, we must endeavour to discover whether the morbid change started in the younger and central cells, or in the mature circumferential cells. And lastly, we must try to determine the most difficult

point of all, the exact nature of the first change, whether it occur in the living or in the formed matter of the cell, and what is the essence of the phenomena which constitute the earliest departure from the normal state, which form the first of a long series of alterations, beginning in health, but gradually leading away from that state to culminate in, perhaps, an extreme departure from the healthy state, actual disease.

The Liver-Cell.—From Healthy to Morbid Action.—The account I have given of the "liver-cell" will, I hope, have led the reader to take a view of the nature of this body, and of its action and changes in health and disease, somewhat different from that which is generally entertained. We must endeavour to realise the phenomena which follow in order, from the time when each elementary part is formed by division of the bioplasm or nucleus of a pre-existing one in the central part of the lobule to the disintegration of the formed matter, which results at last when the cell has reached the peripheral portion of the cell-containing network.

In this organ, as in the case of other organs and tissues, the earliest and most obvious departure from the normal condition which manifests itself, is change in the size of certain cells, and this change, beginning in one or two cells, may soon affect a large number, until nearly all the cells of the lobule may be considerably larger or smaller than in health. In some cases the change in size is pretty uniformly distributed; in some it is limited to the marginal, in others to the central, cells. In some cases a few cells here and there seem to take up more or less than their share of nutrient matter, and become larger or smaller, while in those near these no change can be observed. The rate of change into biliary and other matter which the formed material of the cell undergoes varies greatly in different cases and at different times in the same organ.

Besides changes in the size of the liver-cells, great alterations are observed in their consistence, for the matter at the outer part of the cell, if not that within, may become much harder or softer than it is in the normal condition.

The change in size of the liver-cell is sometimes very considerable. The cell may be increased to three or four times its ordinary size, or it may be reduced in considerable degree, but in each extreme the change in size may be accompanied by irrecoverable departure from the normal condition. A certain degree of enlargement or reduction in size, however, is not inconsistent with health—indeed during life the cells frequently vary in dimensions from time to time, according as function is quickly or slowly discharged. Within the physiological range an individual cell probably alters in size and at a different rate at different periods of its existence. Generally, a greater degree of change occurs in the fully formed cells near the periphery of the lobule, which are

most active, than in the small ones at the centre, which are growing but not discharging function. In amyloid degeneration, however, the enlargement of the central cells may be enormous, and often far exceeds any alteration in size affecting the cells in any other part of the lobule under any circumstances. The marginal cells probably attain their largest dimensions in certain forms of fatty liver, in which the fat forms large masses, almost like those of ordinary adipose tissue. The fat is formed by the living matter of each cell, and gradually accumulates until a large oval mass of uniform consistence and composition results. In some cases almost all the hepatic tissue disappears, and a section of the liver closely resembles a section of adipose tissue. Some of the oval masses of fatty matter are as much as the 1-1000th of an inch in long diameter. Cells thus altered may be reduced in size by the removal of some of the accumulated fat, but they can never regain their former characters, or again discharge their proper function.

Even in health very wide differences exist in size between the elementary parts in different portions of the cell-containing network. Although it is true in a general way that the smallest are found near the central, and the largest near the circumferential, part of the lobule, in many instances considerable variation in size obtains in every part, and the same cell undergoes considerable alterations in size at different times, according to the varying activity of the gland. Some elementary parts are twice or three times as large as others, while not a few may be regarded as one mass, dividing into two or more, or as composed of several small elementary parts in juxtaposition.

The alterations in the action of the liver-cell within the limits of health are very remarkable. These involve not only change in the rate, but in the character, of its action. Even as regards the biliary colouring matter alone, the most striking differences are observed. Sometimes it is nearly black, sometimes brown, sometimes of a bright and very light yellow, while varying shades of green are exceedingly numerous. It is not very unusual to find small particles of inspissated colouring matter in the outer part of many of the liver-cells at the margin of the lobules, and occasionally well-marked dark crystals of bilirubin are present. The varying colour of the fæces is in great measure determined by differences in hepatic action. The bile produced may even be black. It may well be asked whether this striking change in colour is due to changes in the cell before or during the secretion of bile, or depends upon changes in the bile after it has left the cell, and while it is flowing along the ducts. The fæces are sometimes very dark—are indeed almost as black as they are found to be when the colour is due to the presence of iron or blood. They may be almost white, of various shades of yellow, brown, or grey; and this variety in colour is due chiefly to variation in the quantity and composition of the bile.

The bile-forming properties of the cell may preponderate in one case, amyloid in another, fat formation in a third, albuminoid transformative action in a fourth. Thus we may have different kinds of hepatic derangement, and, as would be supposed, a great variety of symptoms is experienced by those who suffer. Disturbed digestion, chilliness, depression of spirits, feeling of nausea, loss of appetite, flatulence, sense of fulness, tenderness and actual pain, diarrhœa, or obstinate constipation, may be experienced.

If we study the cell changes which occur in the borderland between health and disease, and try to realise how pathological succeed to physiological phenomena, we shall, I think, be led to the general conclusion that morbid action most frequently begins in disturbance of the normal rate of cell changes. The cell lives too fast or too slowly. And when disease has actually occurred it will be found that cell life has been carried on for too long a time at a rate departing considerably from the normal on the side of excess of deficiency. If there has been excess of action, the bioplasm of the cells may grow and divide and subdivide so quickly that there is not time for the production of any formed material at all. The liver ceases to discharge its function. The cells multiply in number, and a rapidly growing cell tissue, which is at length destitute of any bile-forming power, results.

But, as I have already remarked, the disturbed action of the liver-cell may be due to alterations in the blood flowing through the adjacent capillaries, and the pathological action instead of beginning in the liver-cell may be said to begin in the blood, the cell being influenced only through the alterations in the circulating fluid. In some cases the liver-cell fails to act as in health upon the blood, and this failure causes noxious matters to accumulate; in other cases the blood is first changed and the cell changes are only secondarily induced.

The cell-containing network of the liver may slowly degenerate, and at last a "connective-tissue corpuscle" may be all that remains to represent a portion of the cell-containing network. In such cases the entire organ is reduced to a form of passive tissue, with here and there the remains of vessels, cells, and other anatomical elements. If great care be taken such extreme degeneration need not be fatal, and, particularly if the patient is already extremely emaciated, his life may be considerably prolonged if he is careful.

DISTURBANCE COMMENCING IN THE CAPILLARY CIRCULATION.

When the physician carefully considers the arrangement of the several anatomical elements which has been referred to, he will not feel surprised that slight disturbances in the flow of the blood in the portal vein, and alterations in its composition, may occasion considerable

departure from the normal action. Rather when he reflects upon the extreme irregularities as regards the quantity and nature of the food introduced at different periods into the alimentary canal, will he not wonder that the elaborate arrangements existing in the liver under any circumstances last as they frequently do during a long and active life without serious derangement or deterioration? As already remarked, the organ will bear a great deal, but to the pernicious system of having day by day far more work forced upon it than it can discharge it at last succumbs.

In most cases of functional derangement of the liver, there can be little doubt that a very early step in the order of change is the retardation of the circulation of the blood in the portal capillaries at the margin of the lobule, in consequence of the cells not being able to remove fast enough from the surcharged blood the materials just absorbed from the intestinal surface.

After a time the rate of flow of the blood becomes very slow and the vessels become disturbed. Some small proportion of blood does no doubt traverse the capillaries and gain the hepatic vein. This imperfectly depurated blood circulating in the systemic vessels occasions those derangements which are so common in persons who suffer from injudicious eating and drinking.

Nevertheless it must be admitted that, as regards the capacity of the liver for effecting change and the rate of its action, the greatest differences prevail in different individuals. Some livers are able to discharge twice or three times the amount of work in a given time that others are capable of. And it must be borne in mind that very free action of the liver-cells promotes free blood circulation through the capillaries, and that this favours free circulation in the capillaries of all parts of the intestinal canal. We cannot account for this simply by the larger size of the liver. It seems to me that we must assume that the liver-cells of some individuals are more active and are capable of doing more work in a given period of time than those of others. In some persons the liver is relatively larger than it is in others, and is therefore capable of doing more work.

When, however, the liver frequently varies considerably in activity, the change is perhaps mainly due to altered action in the nerve centres, which influence and regulate the blood flow, but in most cases the irregularity in action is only in part due to this circumstance. It would seem that in some there is an exceptional activity in the cells themselves, which may possibly be inherited. The different glands in the body and, of course, the gland cells, as well as the muscular and nervous elements, exhibit very varying degrees of activity and capacities for action in different individuals. These, like other individual traits of remarkable or peculiar character, are hereditarily transmitted, and are

clearly not of physical or chemical origin, but are essentially vital in their nature.

The physician must not forget that the most powerful and most constantly active organs may be strained by overwork, so that after all it is doubtful whether an organism with exceptionally active organs invariably enjoys a real advantage, inasmuch as the consciousness of possessing exceptionally active and powerful organs may act as an incentive to overtax them, and thus they become subjected to strain and are damaged.

A congested state of the capillaries is not commonly uniformly distributed in the central and peripheral portions of the lobule. In one case the capillaries near the surface may be much congested, while those in the central portion contain less than the usual quantity of blood. In another the area of congestion is completely reversed. Now with regard to the peripheral part of the lobule, it is to be remarked that, if the secreting cells have recently absorbed a considerable quantity of material, their bulk will be so much increased that they will press upon the capillary vessels, and thus prevent them from being distended with blood. This state of things would cause congestion of the portal vein and intestinal vessels.

In cases in which the onward flow of venous blood to the right side of the heart and through the pulmonary capillaries is retarded or interfered with, the intralobular veins and the capillaries opening into them will be much distended, and if in such a case the cells in the peripheral part of the lobule should be enlarged, blood will accumulate in the capillaries near the centre of the lobule, and this part of each lobule will appear to the unaided eye to be red while the circumference will be pale. Each lobule will seem to consist of a red substance in the centre with a layer of pale tissue around it, an appearance which led some of the older observers to think that each elementary portion of the liver was composed of two distinct substances.

Not only is the thorough depuration of the portal blood effectually provided for, but certain matters which are not adapted for absorption by the liver-cell and matters resulting from the chemical changes in the cell itself, and not fitted for conversion into bile or into substances which after being reabsorbed into the blood undergo ulterior changes in the lungs or in other parts of the system, are taken up by the lymphatic vessels. The radicles of the lymphatics, I think, commence in the small spaces which are continually varying in extent which lie between the external wall of the capillary vessels and the delicate thin-walled tubes in which the liver-cells or elementary parts lie. The lymph spaces in question probably always contain fluid, which accumulates and from time to time passes into the lymphatic vessels and is carried away. The lymph spaces are also of importance as being

the seat of accumulation and growth of colourless exudation corpuscles in inflammation, and of the commencement of other important pathological changes.

If the portal capillary vessels become so distended that their walls are considerably stretched, transudation will probably take place, especially into the spaces above referred to. Not only the fluid portion of the blood, but small blood corpuscles and small portions of colourless corpuscles, pass through the temporary rents or fissures in the vascular walls, and accumulate, grow, and subdivide between the capillary wall and the walls of the tubes of the cell-containing network. In some cases the particles of living matter which escape with the liquor sanguinis into the interstices of the hepatic structures grow and multiply very fast, and this circumstance and the rate of their disintegration or conversion into fibroid will determine the rapidity of improvement, the period at which it may commence, and the degree to which it may ultimately extend. That such corpuscles after a time may die and break down, and the resulting products be reabsorbed by the blood, and the organ at length regain its normal state, is, I think, very probable. Nay, we know that the liver may be greatly enlarged and remain enlarged for months and yet return to its normal volume and regain its ordinary activity, facts which can only be accounted for on the supposition that a considerable quantity of material has transuded from the blood, and has accumulated and remained for a considerable time in the interstices of the hepatic tissue. The hardness, the largely increased volume of the liver, lasting for months, and its very gradual decrease in size, cannot be adequately explained on the hypothesis of chronic vascular congestion only, however considerable this may have been. But this very favourable result is, if not exceptional, at least rare. More commonly, soon after the changes above referred to have taken place serious structural change begins, and it may be very slowly progressive, until symptoms render it certain that chronic disease from which recovery is almost impossible has been established.

A more or less congested state of the capillary vessels, whether caused by some defect in the depurating action of the cells or by the accumulation in the blood itself of too large an amount of matters to be separated, with long-continued slowing of the blood flow, constitutes the incipient stage of many changes which determine chronic structural disease. For in such cases the blood cannot be properly or continuously depurated, and it, therefore, accumulates in the capillaries of the lobules and distends them. The portal vein gradually becomes unduly distended, and the blood is then thrown back and caused to accumulate in the intestinal vessels. The process of absorption is impeded, and the contents remain for a long time in the bowels. So far there is no structural change. A physiological or functional derange-

ment, which having lasted for a considerable time, or having recurred again and again at short intervals, may at length become pathological, and result in morbid action and very decided structural alteration. Even this may be remediable for a time, but if it persist for long it will certainly become irremediable. What then is the order of change which ends in structural disease? The portal blood, being very rich in constituents to be changed by the liver, is not as quickly depurated as is needful for the blood to flow through the hepatic capillaries at the normal rate. The cells absorb what they can, and enlarge, but the crude material in the blood cannot be taken up and changed by them fast enough to sufficiently depurate the blood for it to flow freely through the capillaries of the lobule. The cells under such circumstances enlarge while little bile is formed. Indeed the conditions are unfavourable for the disintegration of the formed material of the cell, and its conversion into the special products of secretion. The enlarged cells impede the onward passage of the inadequately depurated blood. The venous engorgement persists, and, if from time to time it lessens, it may become a frequently recurring difficulty, with accumulating and intensified deleterious results. Soon fulness of the right side of the heart and dilatation and weakening of the walls of the right ventricle, short breath, and other disturbances of the lungs follow. There will probably be nausea, and often headache, and indisposition to take food, and frequently flatulence, which adds to the pulmonary and cardiac embarrassment. The whole of the blood in the system is altered, and the nutrition and action of all the tissues and organs of the body will be more or less deranged. The serious changes in question cannot long continue without great interference with the nutritive processes in every part of the body and impediment to the action of the most important tissues. If the patient is fortunate he will lose considerably in weight. His food will be considerably reduced, while steps are taken to promote the more free circulation of the blood, and to ensure its depuration by increasing the action of the kidneys and intestinal canal, at least in the case of persons in whom these organs are in a healthy state. Under favourable conditions and good daily management the patient may live for many years, but he will have to be most careful as regards the food he takes and the way in which he passes his time, if he is to attain the maximum period of life possible under the circumstances. This may comprise perhaps ten or fifteen years, if the acute attack occurred between forty and fifty, but in all such cases the tenure of life is very uncertain. Some unexpected intercurrent malady may cut short life, or an injudicious act necessitating unusual muscular or nervous effort, or over-fatigue, may be followed by sudden increase of pathological change which may be fatal. Still, if care be taken, not only may life be endurable, but the patient may be able to discharge a

considerable amount of quiet useful work. He may feel contented, and even in a certain way may enjoy himself.

Of the Capillary Walls.—The walls of the hepatic capillaries in health are very thin, so as to allow the blood as it traverses them to be readily acted upon by the hepatic cells. Under certain conditions of disturbed circulation or local capillary obstruction, biliary matters and even small solid particles may make their way through into the blood, soon causing jaundice and probably death from blood-poisoning or other changes.

In some forms of disease, after stagnation of the circulation of the blood in the capillaries has existed for some time, disintegration of the slowly coagulating or non-coagulating blood, breaking down of the tissue forming the capillary walls, as well as of the adjacent hepatic cells, has been known to take place, and the *débris* resulting therefrom may occasion the formation of an abscess; or death and mortification of adjacent parts may follow, and this would almost certainly be fatal in the course of a few hours.

In some cases the walls of the capillary vessels are found to be so thin and of such little substance that when empty they fall together in the section under examination. They are, indeed, in many cases actually invisible, unless they are artificially tinted with some coloured material or are made manifest by some minute granules, as of carmine or Indian ink, being allowed to come in contact with them.

Thickening of the Capillary Walls.—On the other hand, in certain pathological conditions the capillary walls increase much in thickness, and, though transparent, become so firm and hard that on transverse section the tube remains open, the walls standing firmly apart. This thickening seems to be due to the deposition from the blood of transparent material upon the inner surface of the capillary wall. It is possible that in some cases the new material deposited may be removed and the capillaries restored to their normal condition, but generally no such favourable change occurs, and the change proceeds until the ordinary hepatic cell change is considerably reduced or completely stopped.

In amyloid or albuminoid liver, besides thickening of the walls of the vessels, a transparent material accumulates in the liver-cells, and the bile is diminished in quantity and much altered in character, being often very pale and less viscid than in health. Not only is bile formation much lessened in these cases, but the other transforming actions of the liver are reduced or stopped. The activity of the muscular and nervous system is much impaired, and the secerning operation of the various glands is reduced to a minimum, and the composition of their secretions much modified.

TREATMENT OF CONGESTION OF THE LIVER.

The discomfort in the situation of the organ itself and the secondary results occasioned in various parts of the body through the influence of the nerve changes consequent upon the slowing of the circulation and distension of the capillaries of the lobules of the liver have been in some degree experienced by most persons. Occasionally a patient suffers the greatest inconvenience from frequent attacks of perhaps only slight congestion of the liver, and the consequent disturbance of digestion and assimilation resulting from derangement of the bile-forming process, and other hepatic disturbance.

All that is required for a liver enlarged by distension of all its vessels with blood to return its normal condition is rest. Slowly the blood passes through the lobular capillaries, and being partially relieved of the substances which should be entirely removed from it by the cells, the accumulation which has retarded the onward progress of the blood toward the hepatic vein is reduced, and tension and pressure are relieved. Gradually the blood flows through the capillaries at its ordinary rate, the whole organ is reduced in volume, and the attack is over. But, if this favourable change is to occur and to continue, it is obvious that absorption from the intestinal surface must for a time be reduced to a minimum or cease. In other words, little or no food should be taken. But, if the state of the patient is such that temporary starvation would be dangerous, food in very small quantities at definite intervals must be given, and of such a kind and in such a form as will give the liver the least amount of work.

Rest to the liver means of necessity rest to the stomach, rest to the small intestine. If food is allowed to enter the stomach, it must pass on into the small bowel, and while there much of its soluble constituents will be absorbed and carried to the liver, and this organ will have to work or to suffer from congestion and accumulation of blood in its capillaries. Not only will it suffer from the accumulation of blood and consequent alteration and disturbance of the action of the cells, but under the conditions supposed the crude and improperly prepared material will be carried to the liver and do harm to the organ, not only disturbing its secerning action at the time, but possibly exerting a deleterious influence on the cells themselves, from which they would recover very slowly, if indeed they recovered, for it is doubtful whether cells which had been for so long deranged could be restored to their perfectly normal condition.

A patient who had once suffered such an attack should gradually acquire the habit of taking the smallest quantity of food necessary to

keep up his nutrition without loss in weight. To reduce the work of the liver to the greatest extent consistent with the bodily health, and for a considerable period of time, is its only chance of return to its normal state. In many cases, even after the lapse of two or three years, there may be evidence of disease and there may still be considerable enlargement of the liver.

But in advocating rest to the liver and stomach the practitioner must bear in mind the strong prejudices of the patient, and, indeed, of the public. For how many think that life cannot be properly sustained if the individual submits to fast even for a few hours? Whenever this fear of the dire consequences of anything approaching starvation is expressed, the practitioner will do well to consent to allow bread and broth, or weak milk and water, or weak beef tea and biscuit, in small quantity once in three hours, rather than run the risk of exciting rebellious opposition to his advice to withhold all food for a time. And it must be borne in mind that in many of these cases the "rest" required must extend over some weeks if any real and lasting good is to be obtained. By judicious management for a few days some relief may be obtained, but nothing like cure can be hoped for if the liver has been overworked for any length of time.

The diet then must be properly regulated, and while it is obvious it should be "light" and should contain little nitrogenous matters, nothing can be more unwise than to lay down hard and fast rules based upon theoretical considerations. The practitioner must consider how his patient has been living, and in most cases must not be too sudden or too thorough in the restrictions he considers it right to impose. The days ought to be past when doctors deem it necessary to lay down the law as to eating and drinking in an arbitrary and consequential way, laying great stress upon very minute and particular directions which to a sensible person with physiological knowledge will appear perfectly ridiculous. Nevertheless it must be admitted that a large number of patients do find solace, and fancy they discover wisdom, in the injunctions they receive as to the number and exact dimensions of the pieces of bread and butter that they are to eat at a meal. Absurd injunctions laid down very solemnly are unquestionably prized by a certain class of invalids, but this is scarcely a sufficient excuse; for an intelligent adviser has surely higher and better work to do than frame minute directions to please the fancies and caprices of silly people.

Very little meat should be taken in these cases, and alcohol should be altogether forbidden. Our advice should not, however, be too strict, for in the case of persons who have long been in the habit of living freely it is very important not to suddenly impose severe restrictions, or the change may be followed by serious derangement or a very

low state of health, which may be succeeded after a time by some intercurrent malady which may prove fatal.

The natural return to the normal condition as regards the circulation in the liver may be promoted in another way. It has been incontestably demonstrated that if the glands of the intestinal canal be caused to act freely, and the removal of water, especially from that portion of the blood which is circulating through the intestinal vessels, be quickly effected, the flow through the hepatic capillaries will be promoted. In many such cases the practitioner is well aware that the congestion is not limited to the hepatic vessels, but that those of all the internal organs are in a similar state. Sharp purgation in the first instance and then frequent moderate action of the bowels afford quick and thorough relief. We have a large number of remedies from which to select. One of the most useful, quick, and certain in its action is castor oil, so wisely employed by our predecessors, but jalap, scammony, podophyllin, elaterium in small doses (one-twelfth of a grain carefully mixed with compound colocynth pill), or some other purgative preferred by the practitioner. Saline purgatives, and especially the sulphate of soda and sulphate of magnesia, potassio-tartrate of soda, are of great advantage when very decided or immediate action is not required. In those numerous cases in which the congestion is almost chronic and, from the way the patient is in the habit of living, inevitable, the latter are most valuable and undoubtedly prolong life. Large eaters, and especially large meat eaters, often take an active saline purgative almost daily, and not a few find that free purgation alone relieves them from the serious discomfort which generally attends upon indulgence in eating and drinking. A few probably consider this a small penalty to pay for the free and frequent indulgence of the appetite. I knew a very large eater who began the day by eating about a pound of steak for breakfast, and who kept himself alive till nearly eighty by taking daily an ounce of Epsom salts and a good dose of infusion of senna.

Although a congested condition of the capillaries of the lobule may have persisted for a considerable period of time—nay, though there may have been exudation and the escape of living particles from the blood through the capillary walls—though the liver should have increased to as much as twice its normal size, and had undergone little or no alteration in its dimensions from day to day or from week to week—it by no means follows that the changes that have ensued may not, at least in some cases, be checked, and the organ slowly restored to its healthy state. The real and lasting benefit which frequently results from even a short course of washing out, with judicious attention to diet, and the importance of free exposure to good air and properly regulated gentle exercise, suggests the general plan to be followed in

the case of those who are precluded from enjoying the advantages of a course of treatment at Carlsbad or other place where suitable waters may be taken at their source. If, on the one hand, we study the *rationale* of the health course, and, on the other, observe the results attending the same plan of treatment at home, we need not despair of being of some use to patients who are compelled to remain in this country, and are unable to give up their work even for a week. The use of Glauber's and many other salts was perhaps better understood by a former generation of practitioners than it is by us. In such cases, the old fashion of prescribing two or more teaspoonfuls of Glauber's salts in tepid water once or twice a day was without doubt of great use, and I think that remedies of this class are in these days too seldom prescribed. It is not only persons who are actually suffering from disease who are benefited, but I have no doubt that many who are as it were preparing themselves by injudicious living for chronic liver disease would escape if, before actual morbid change had resulted, they were enjoined to take frequent doses of saline medicines. Carlsbad water, natural and artificial Carlsbad salts, may now be obtained without difficulty in London. Many salts which have a diuretic and slightly purgative action are very valuable in the treatment of enlarged liver, at least during the early periods of the disease, and a mixture of three or four salts will often be found more useful than sulphate of soda or sulphate of magnesia alone. In treating those who cannot leave, or are too poor to profit by a visit to Carlsbad, the following mixture may be prescribed with advantage :—

Sulphate of Soda	4 oz.
Sulphate of Magnesia	1 oz.
Chloride of Ammonium	¼ of an oz.
Nitrate of Potash	¼ of an oz.
Chloride of Sodium (Common Salt) ...	1 oz.

To be powdered and well mixed together, and kept in a wide-mouthed, well corked or stoppered bottle.

Dose—a teaspoonful or more in half a tumbler of tepid water, twice or three times daily (an hour after breakfast, about 4 o'clock, and an hour before going to bed) for a week or ten days at a time.

But, at least in many cases, it is not even absolutely necessary to give salines or any other medicines. Drinking a considerable quantity of water, or barley-water, or linseed tea, during the day, and persisting in the plan for a few weeks at a time, often affords great relief. A quart of water daily, divided into half-pints, taken at pretty equal intervals between the meals, will sometimes be of great use. The water may be flavoured with lemon juice; and if it contain carbonate of lime in any quantity, and of course if there should be any doubt as to its purity, it should be well boiled for a quarter of an hour and allowed to

cool before it is taken. Or some form of "Soda water" (Geraut and Cos'. syphons of soda water are very convenient), or "Apollinaris water," or "Brighton Seltzer," or "Salutaris," which consists of distilled water made effervescing with a considerable excess of carbonic acid, may be taken in preference to ordinary water, and without any risk of disagreeing.

Mercury.—Of all the remedial substances which have been found to be of use in chronic simple enlargement of the liver, there is at any rate no single preparation which in potency comes near to mercurial preparations, if properly used. Whatever may be the precise manner in which mercury acts, there can be no doubt of its usefulness. Our fathers, perhaps, sometimes may have used the drug injudiciously, and may have attributed to it virtues which it does not possess, but, broadly, they were certainly correct in attaching great importance to this class of remedies in the treatment of the condition we are considering. Nor must it be supposed that we use little or no mercury in these days, for there is a widespread idea not only that mercury is the remedy for syphilis, which is unquestionably true, but that diseases in which the drug is beneficial are due to syphilitic taint, direct or inherited, which is not true. The fact of great improvement under the exhibition of mercury given exactly as if the case were syphilis is no proof whatever that the disease is of this nature. The beneficial action of mercury in some forms of derangement of the stomach and bowels, and upon the neoplastic materials in the substance of the liver in enlargement of that organ, is due, no doubt, to the same properties which make it so valuable in the treatment of special changes. But many practitioners have, I think, gone much farther than the facts warrant in concluding that mercury exerts an influence in syphilitic affections of a kind different from that produced by it in many non-syphilitic maladies; while the dictum that improvement under mercury or iodide of potassium or other iodide may be accepted as evidence of the syphilitic character of the disease is altogether unjustifiable.

The beneficial effects of mercury are probably due to the influence this substance exerts in promoting the absorption of exudations in the interstices of tissues. The precise way in which it acts has not yet been made out, but that recently effused lymph is more quickly taken up when a patient is taking small doses of mercury is quite certain. Not only so, but in cases where slight injury has caused local exudation in a tissue the favourable effects of a very small dose of mercury may be experienced. Whether the mercury has any direct action, or whether the absorption of exuded matter is due simply to the free secreting action produced by the remedy on almost all the secreting glands of the body, is not conclusively determined. The beneficial effect of mercury has been experienced by so many and in such a number of morbid

conditions that no doubt can be reasonably entertained of its efficacy. For the relief of those very unpleasant feelings, usually attributed to "biliousness," nothing comes near it, and it is certain that it produces an effect upon the liver. When the liver is congested and is the seat of exudation, mercury, judiciously given, is invaluable.

In chronic simple enlargement of the liver, especially when exudation has occurred, there is no doubt that small doses of perchloride of mercury (one-thirty-second to one-sixteenth of a grain), half-an-hour after food, is a most useful course of treatment to pursue. I generally prescribe the liquor hydrarg. perchlor. of the Pharmacopœia, with four to ten grains of iodide of potassium, and five or ten minims of the extract. cinchonæ liquid., with a few drops of tincture or essence of ginger in an ounce of water, to be taken about an hour after breakfast and dinner, and to be continued for a month at a time if it does not in any way disagree with the patient.

The potency of mercury is much enhanced by giving it in conjunction with pepsine. So small a dose as one-third of a grain of grey powder, or half the quantity of calomel, with two grains of Pepsina Porci (Bullock and Co.)* in the form of a pill or powder, after dinner, twice or three times a week, is often of very great use. One great advantage of these very small doses of mercury is that the discomfort which often follows mercurial preparations does not result. Another is that when frequent repetition is desirable, as in certain forms of dyspepsia and in many kinds of enlarged liver, there is not the same risk of salivation or of the weakening effects often attending mercurial treatment.

Mercury may be introduced into the system by the mouth or by inunction, or by being reduced to a state of minute division by volatilization and absorbed by the skin in a vapour bath; and salivation and other effects of the drug may be thus produced. But the value of mercury is not shown by the fact of the occurrence of salivation; indeed, as we now use the drug, we endeavour to prevent this objectionable and exhausting action.

In all cases of enlargement of the liver, whether or not accompanied by pain, and more especially if the enlargement is recent, the greatest benefit results from the use of linseed-meal poultices, or spongio-piline or ordinary fomentations, and other moist applications over the region of the liver. A wet compress answers perfectly well, and may be applied for many hours daily. Two or three thicknesses of lint or rag eight or nine inches square, wrung out in warm water, will answer perfectly well. The application should be covered with a piece of thin mackintosh or oil silk, and the patient will not be in any way inconvenienced by it. It must be worn day by day perhaps for months. Should the cuticle get soft and tender, the patient may give it up for a few days,

* See "Slight Ailments," Second Edition.

and then resume its use. Occasional counter-irritation may also be tried. Mustard, iodine, and other counter-irritants have been used, but care must be taken to avoid injuring the skin. Except in the case of actual pain, which may undoubtedly be relieved by sharp irritants applied for a short time, or by the application of a few leeches, the counter-irritation should be gentle, and repeated at short intervals. In chronic congestions and inflammations it is to the repeated application of slight counter-irritation over an extended period of time that we must look for benefit, and there is no doubt of the value of the treatment conducted according to this principle. The older physicians used to rub in mercurial ointment, or iodide of mercury, but, except in very chronic cases, harm rather than good may result from assiduous friction. The value of rubbing was in former days much exaggerated, and in the enthusiasm for promoting the free circulation of fluids in the tissue interstices, there is, in these days, some danger of organs in a state of chronic inflammation and enlargement, which require perfect rest, being injudiciously subjected to pressing, rubbing, kneading, or squeezing.

GALL STONES, JAUNDICE.

Biliary matters may accumulate in the substance of the liver-cells as minute crystals or variously shaped yellow or green granules or globules in and around the cells, in the ducts, and in the gall bladder. When biliary matters are deposited in the liver-cell, it is probable that the substances formed by the cell are converted too soon into biliary constituents which collect in the substance of the cell, instead of undergoing change into biliary matter at the time of or after their escape from the cell.

The solid constituents of the bile, like those of the urine, are sometimes formed in a highly concentrated state, so that, if a little more of the water which holds them in solution be absorbed, crystals may be formed, or solid matters, which, having been once produced, increase by the deposition of new matter on the outside, until concretions sometimes of considerable dimensions result. As I have already remarked, in every part of the biliary ducts, from their commencement as very fine thin walled tubes to the gall bladder or to the opening into the duodenum, is an arrangement for favouring the concentration of the secretion.

Under normal circumstances the bile is formed in a very diluted state, and from the moment it leaves the cell, the seat of its production, it begins to undergo change, much of the water being gradually absorbed. The bile may vary in colour and consistence irrespective of any morbid changes in the liver. In other words, it would appear that under slight alterations of the condition bile of very different character may be secreted.

No wonder that in many cases concentration is carried on too

quickly, and proceeds so far that the bile will scarcely flow along the ducts. Sometimes this viscid bile as it lies in the smaller ducts undergoes further concentration, and becomes quite firm and hard, completely obstructing the duct in which the hard matter has been formed. From the arrangement of the ducts, these elongated cylindrical masses of concentrated bile when removed much resemble a branching twig. Occasionally such are found in considerable number, and may lead at first to dilatation of the ducts, and afterwards to wasting of the secreting structure of the lobules, corresponding to the duct or set of ducts obstructed.

Changes often take place in the bile if it lies too long in the ducts and gall bladder. Chemical decomposition occurs, and when after a time a quantity of this altered bile is discharged, its irritant properties may be sufficient to produce soreness and excoriation about the anus. In fatty liver the bile generally loses its ordinary characters, and a fluid may be found in the gall bladder which is altogether destitute of the resinous acids, and consists principally of mucus, albuminous matters, and crystals of phosphates.

While then there is no doubt that the formation of biliary, like that of urinary, concretions may be favoured by a small proportion of liquid to the solids of the food, it is certain that this is not the full explanation of the formation of gall stones. The tendency to the formation of biliary calculi is very pronounced in some individuals and in some families. Like urinary calculi and gouty deposits, the affection is not entirely dependent upon the food. At the same time one may feel perfectly sure that a moderate diet with a considerable amount of liquid, and free action of the organs of excretion, would tend to prevent the formation of gall stones in one predisposed thereto, while the opposite state of things would contribute to their production.

Deficiency of fluid in relation to secreting processes will not in many cases account for the formation of highly concentrated secretions and deposits of solid matter. And although undoubtedly in many instances a large amount of highly nutritious food in proportion to the quantity of water taken is associated with the presence of conditions favourable to calculus formation, it is quite certain that this cannot be accepted as an explanation of the fact generally applicable. In some cases the formation of a stone seems to be almost contemporaneous with the commencing activity of the gland itself, the process therefore occurring long before it is probable that concentration of the secretion can take place. Biliary calculi have been in fact formed during intra-uterine life long before birth, and have been found impacted in the gall duct, which was obstructed to a degree sufficient to cause jaundice.

Gall Stones.—While then inspissation of the bile plays an important part in the formation of some gall stones, and of certain hard matters

found in the ducts of the liver and in the gall bladder, solid substances are undoubtedly produced altogether independently of this process. Certain hard concretions unquestionably consist of highly inspissated bile, which has afterwards very gradually become quite hard in consequence of the further very gradual removal of water. Other forms of solid matter seem, however, to be due rather to the precipitation of a crystalline substance previously held in solution, in consequence of chemical changes in the compounds, by which the precipitated matter had been dissolved. If, as was shown by Thudichum, normal bile be kept for a year or more in a perfectly closed vessel, it will become acid, and a granular sediment will be thrown down. In the corresponding changes occurring in the ducts during life, and resulting in the precipitation of biliary sand, probably bacilli are concerned. Decomposition of the salts of the bile also causes the cholesterine to be precipitated, and as many gall stones contain upwards of 80 per cent. of this substance, it is obvious that the formation of calculi of this kind cannot be due to concentration of the bile.

The material of which the gall stone is mainly composed differs remarkably in different cases. Some gall stones consist chiefly of inspissated bile, with portions of altered epithelium and other substances embedded, while it is not uncommon to find a gall stone composed of almost pure cholesterine, perfectly colourless, and exhibiting the characteristic crystalline fracture.

Cholesterine is a very light crystalline substance belonging to the alcohols, but it is heavier, not lighter, than water, as some supposed. Its specific gravity is above 1000. Although gall stones, and particularly those which have become very dry by having been long preserved in museums, will float upon water, being buoyed up by air imprisoned in the interstices between the crystals, moist gall stones of all kinds will be found to sink in fresh water. Very large gall stones are occasionally met with, some having been found more than three inches in length, and stones of more considerable dimensions are recorded. Buisson speaks of one the size of a hen's egg (quoted by Thudichum). Dr. Burt described a stone which weighed as much as three hundred and twenty-three grains when dry, and gall stones weighing more than an ounce have been found.

Cholesterine is soluble in hot alcohol, in ether, chloroform, and benzole. In the bile this substance is dissolved by the glycocholate and taurocholate of soda. Whether cholesterine is actually formed in the liver is doubtful, seeing that it is present in all parts of the nervous system, and results during the morbid changes known as fatty degeneration in various tissues and organs. It seems, therefore, more probable that cholesterine is taken from the blood by the liver-cells, dissolved in the bile, and at last removed from the body with other substances in

the intestinal canal. Some observers seem to think that the cholesterine is somehow formed by the mucous membrane or secreted by small glands, but it is now certain that the cholesterine is slowly deposited from its solution in the bile. Sometimes the cholesterine is pure, and sometimes mixed with epithelium and biliary matters. Some specimens of bile are much richer in cholesterine than others, but what the conditions may be which favour the formation of a large quantity of this substance is unknown. A large amount of cholesterine is invariably present in the brain, spinal cord, and nerves, both in health and disease. Cholesterine exists in many other tissues of the body as age advances, and in certain degenerative changes is found in textures in which it is not present in health. An invariable constituent of human bile, cholesterine is not present in the bile of the ox, sheep, and many other animals.

The Nucleus of Gall Stones.—In the formation of a biliary calculus some small insoluble particle deposited from the bile or resulting in some other manner is the first step. The insoluble matter often consists of epithelium, but the real nature of the nucleus of many gall stones was first demonstrated by Dr. Thudichum, who showed that almost invariably, if proper precautions were observed in dissolving the hard matter of the central part of gall stones, small elongated hair-like bodies, usually branched, were discovered upon microscopical examination. These were generally of a dark colour, and were for the most part composed of inspissated bile, mucus, and epithelium. They were clearly casts of very small ducts, and in many instances several had collected together. In consequence of chemical change in the taurocholate of soda which dissolved the cholesterine, the latter substance was set free and deposited amongst the little collection of entangled casts of the ducts. In this way a very small calculus or portion of "grit" or "gravel" not deserving the name of stone is formed. Layer after layer consisting of cholesterine or of inspissated biliary matter, and more commonly of both, is slowly deposited, and the stone gradually increases in size. Sometimes a number of these minute casts of the ducts, most of them being less than the 1-200th part of an inch in diameter, would by the pressure of the accumulating bile behind be forced onwards from the minute ducts in which they were formed into ducts of a larger size, where several would collect together, and longer ones intertwining and becoming entangled a small collection would soon be formed. Mucus, epithelium and epithelial *débris*, and any minute solid particles would adhere to them, and gradually a small rounded mass of considerable firmness would be formed, upon which the least soluble ingredients of the bile would be slowly deposited. Of all the substances in bile, cholesterine is that which probably most readily passes from solution, and is deposited in comparatively insoluble crystals. When

once a thin layer of this substance has formed on the outer surface of the mass the further deposition is certain. The microscopic crystals already

Casts of biliary ducts obtained from the central part of gall stones, and constituting the nucleus of the concretions. × 80. From Dr. Thudichum's "Treatise on Gall Stones," 1863, p. 63. The engraving kindly lent by the author.

formed favour, if it may not be said attract, more crystalline matter, and so increase proceeds. Thus may several stones be formed, which one

by one may pass into the gall-bladder, where they further increase in size. As the stones become larger they rub more or less against one another, so as to determine the deposition of new matter in certain situations rather than uniformly all over each one. According to their number and the positions they are made to take with respect to one another, the stones may take a tetrahedral, a cubic, a polyhedral, a spherical, or an oval form.

A little pellet of viscid mucus, a collection of epithelial cells, entozoa, or fragments of dead entozoa, particularly the fluke, have been found to be the starting-point of a biliary calculus. When a nucleus of solid matter has in any way been formed the deposition of solid material soon takes place around it, and the calculus increases in size.

Sometime after a stone has been formed, water continues to be gradually absorbed, and contraction not always regular or uniform in all parts of the concretion takes place. Indeed, in some cases, actual fracture and partial disintegration of the stone appear to have been thus brought about. Not only so, but very long after the stone has been formed, owing to some change in the character of the bile, part of the outer surface may be eroded here and there to some depth. Stones are sometimes found the outer surface of which is irregular, being worn away in greatest degree where the stone is softest. The "waterworn" appearances observed have naturally led to the suggestion that this change may be brought about during life if the use of proper diluents were persisted in for a sufficient length of time, but, as far as observation has yet gone, it cannot be said there is much to justify the hope of so desirable a result being attained.

Jaundice.—My distinguished predecessor and master, George Budd, thought that a large number of cases of jaundice were due to the suppression of the secretion of bile, or to defective secretion on the part of the liver, and that the substances which under ordinary circumstances became bile remained in the blood and coloured the tissues just as if bile formed in the liver had passed into the blood. Certain colouring matters, much resembling those in the bile, are undoubtedly found in the blood, and by them neighbouring tissues, as well as the skin itself, are often stained of a deep yellow colour, very like that imparted by actual bile, though the colouring matter is really very different.

We may now regard it as certain that actual biliary matters can be formed by the liver-cell only. It is this body alone that possesses the power of forming the characteristic colouring matters and resinous acids of the bile. Many experiments have been made and facts advanced with the object of proving that jaundice may result from blood change only, as well as from the reabsorption of bile formed in the liver. That, in consequence of certain changes in the matter of the red

blood corpuscles, a yellow colour may be produced, something like that of bile, is quite certain. The observation of the colour changes occurring in an ordinary bruise are convincing on this point. Moreover, a yellow colouring matter, and sometimes minute dark yellow crystals, may be discovered in the seat of extravasations of blood, and not unfrequently just outside capillary vessels which have been the seat of stagnation of blood yellow granules and crystals are found.

It has been held that some of the substances which under ordinary circumstances would be converted into bile by the liver-cells may remain in the blood and nevertheless give rise to actual biliary matter without passing to the liver at all. It has also been contended that bile, or, at any rate, some of its principal constituents, are being continually reabsorbed from the intestine after having been poured into it; but then we must remember that during the process these substances are much changed. Indeed, there is no good reason for concluding that it is by such circuitous course the biliary matters which cause jaundice ever find their way into the blood. If the tissues of any part of the intestine are stained yellow, it is from biliary matters having been carried to them by the blood, not by passing directly through the intestinal walls from the contents as they pass along the bowel.

Some of the biliary constituents, and especially the coloured ones, may be seen in the substance of the liver-cell, and there can be no doubt that the very remarkable chemical substances characterising biliary matter are actually formed through the agency of the special living matter of the liver-cell, and cannot be produced under any circumstances in other cells or in the blood. In some of the lower animals, the blood of which is colourless, the hepatic cells secrete a highly coloured material, as dark and as distinctive as that formed by creatures which have red blood.

I think, therefore, the broad conclusion must be accepted, that jaundice invariably depends upon the presence of biliary colouring matter which was formed by the liver-cell and, instead of being discharged into the intestine, has been somehow taken into the blood and carried to all parts of the body by the circulating fluid. Normally, much of the bile formed in the liver is, no doubt, reabsorbed into the blood—not as bile such as passes into the blood in jaundice, but bile which has been completely changed and altered by the secretions of the intestine, and by some of the constituents of the food. The material has, in fact, ceased to be bile, its important constituents, as well as the biliary colouring matters, having been so completely changed that tissue staining could not occur.

With reference to the manner in which the bile formed by the liver-cell is introduced into the blood, it is a question whether the bile passes directly from the duct into the capillaries or is taken up first of all by

the lymphatics in the liver, and reaches the blood mixed with lymph and chyle. It is possible it may reach the circulation in both ways, but in most cases it gains the blood by a comparatively short route. After an obstruction to the flow of bile along the duct has existed for some time, the most yielding and thinnest portion of the very fine ducts, and the vasa aberrantia and communicating branches, as well as the very thin walled tubes directly continuous with the cell-containing network being stretched, would permit bile to pass through very readily into spaces outside, and come in contact with the adjacent delicate capillary vessels and plexuses of lymphatics.

In that form of capillary hæmorrhage which is commonly met with in the intestinal canal in cases of cirrhosis, very free bleeding often takes place over a very considerable area of mucous membrane, but entirely from the capillaries themselves, in the walls of which longitudinal rents or fissures have resulted from the stretching to which the vascular walls have been subjected. Through these fissures red blood corpuscles would readily escape. Hæmorrhage from capillaries sometimes occurs in the brain, in the retina, in the kidney, and from capillaries in other tissues. One can conceive that in such cases of stretching of capillary walls bile which contains no corpuscles could easily pass into the vessels in an opposite direction through much smaller openings, or even through the extended capillary wall in which no real opening at all existed. The blood soon becomes contaminated with sufficient bile to cause jaundice from tissue staining. While in some cases (acute yellow atrophy) the cells themselves break down and biliary matters, imperfectly formed bile, and the *débris* of the disintegrated cells enter the blood, causing fever and the most serious general symptoms followed by coma and death.

The rapidity with which the staining of tissues is effected after the obstruction to the onward flow of the bile has taken place is different in different cases, and the order in which the textures in the body are stained is not invariably the same. One of the first situations, however, in which the yellow colour becomes pronounced is the sclerotic, but the staining of the skin occurs very early. The fibrous tissues from their whiteness, rather than from any real affinity for the colour, show the slightest change in colour. As soon as the urine becomes yellow the epithelium of the kidney is tinted, and almost anything in the uriniferous tubes may be also coloured. Some tissues seem to accumulate the colouring matter of the bile from the fluid in which it is dissolved, so that the tint of the tissue is deeper than that of the fluid which tints it. Thus the transparent material of a hyaline cast is often stained of a deep yellow colour although the urine may not be deeply impregnated with bile. Many of the imperfectly soluble salts are often distinctly coloured. Muscles and even bones receive a yellow tint in cases in which jaundice

has lasted for a certain time. The coats of arteries and veins, gland structures, and indeed all the textures with more or less readiness take biliary colouring matter. As before remarked, a yellow colour is sometimes observed in the tissues just outside the vessels, but this depends upon changes in the hæmoglobin of blood corpuscles which have escaped through the capillary walls and is very different from the staining caused by biliary matter. The former is usually in very small patches here and there, the latter more or less spread and diffused through the adjacent tissues so as to produce a more uniform staining. After obstruction to the flow of the bile has existed for a few hours the sclerotic is seen to be slightly yellow, and soon the skin has a distinctly yellow tinge, and in the course of a few days the whole surface may be of a golden-yellow, or dark and dusky as well as yellow. The urine varies from a bright-yellow to a dark-green, or almost black if a stratum of an inch or more be submitted to examination. The stools become pale from the commencement of the attack and are usually of a pasty or clayey consistence. In many cases they get nearly white, of an offensive smell, very different from the usual fæcal odour. The colouring matter of the bile dissolved in the urine is imparted to many substances with which it comes into contact. The material of which transparent casts are formed may assume a very deep-yellow colour. The epithelium of the kidneys, ureters, bladder, and urethra are deeply tinged. Even crystalline substances are tinted, such as dumbbells of oxalate of lime, crystals of phosphate; but I have never seen octahedra of oxalate of lime or uric acid crystals thus coloured. Though jaundice is frequently associated with various forms of liver disease which must end fatally, death is not due to jaundice but to other circumstances. In acute yellow atrophy the patient is often intensely jaundiced, and death often occurs within a few weeks after the commencement of the malady, but in these cases there is blood-poisoning consequent upon the product of disintegration of the hepatic cells as well as bile constituents accumulating in the blood. If changes in the cells could be prevented, the patient might live though the jaundice became very intense. For we know that in certain forms of chronic liver-disease with intense jaundice, the patient may not only live for two or more years, but many of the tissues and organs of his body continue to work in spite of being saturated with the yellow colouring matter of the bile. Though he may be very weak and low spirited, his intellect may remain not only clear but active and in good working order, in spite of the brain being continually bathed with blood containing much bile.

Catarrh of the Gall Ducts, Congestion, Ulceration.—The pathological change known as catarrh of the duct resembles catarrhal inflammations generally occurring on other mucous surfaces. There is an unusual abundant formation of epithelial cells with a considerable

quantity of viscid mucus which gradually in passing along the duct is slowly converted into a more or less coherent mass. This may become impacted in the common duct, and may remain there for many weeks before it is expelled by the increasing pressure of the accumulated bile behind it, or it may undergo softening and disintegration, and soon be discharged, any symptoms of obstruction resulting from its presence at once ceasing. It is probable that in the catarrhal state of the duct the vessels of the mucous membrane are congested, and the tissue itself more or less swollen from fluid being poured out in the interstices.

The catarrhal state of the ducts is often associated with a somewhat similar change of the stomach and bowels, and it is probable that in some situations the redundant epithelium intimately adheres to the surface and is firmer and harder than that usually produced. The glands and passages connected with the ducts no doubt also contain mucus. The catarrhal state is sometimes chronic, and, although it is remarkable that jaundice depending upon this cause usually occurs only once in a lifetime, it now and then happens that after the first plugging of the duct has yielded it is succeeded by a second attack, and the jaundice which appeared to be passing off returns with increased severity.

Occasionally, in a case which seems to be due to catarrhal jaundice, a permanent change has occurred. An irregular papillary growth has been formed in the common duct near its orifice. There may be complete occlusion of the duct and intense jaundice resulting therefrom which ends fatally. One of the worst cases of jaundice I ever saw was due to this unusual form of growth near the opening of the common duct. The growth in question seemed to be nothing more than an exaggerated growth of the mucous membrane, with nothing like cancerous structure about it.

As in the case of other mucous membranes, ulceration of the mucous membrane of the gall duct occurs. Short of actual ulceration, local congestion with more or less abrasion of the surface is probably not uncommon. The process may be started by entozoa or their ova; or, some of the capillaries being obstructed, impaired nutrition may result, with the growth and multiplication of bacteria, ending in ulceration. In the case of chronic ulcers which now and then occur after typhoid and other fevers there is exudation into the submucous tissue, with subsequent thickening and formation of fibroid tissue with some puckering and irregularity of the surface. If these processes occur in the common duct there may be thickening and contraction sufficient to cause occlusion. Jaundice of a severe and persistent character will soon occur, and dilatation of the duct will result, to be followed by serious structural change in the hepatic tissue, and death from six

to eighteen months or more after the first commencement of the symptoms.

Obstruction of the Duct from Pressure or Constriction.—Many physicians have concluded that muscular spasm of the common duct, or of the muscular coat of the intestine near the point of entrance of the common duct, has been the cause of the accumulation of bile in the gall bladder and in the ducts in every part of the liver. There is reason to think that congestion of the mucous membrane and effusion beneath it have also in some cases been the cause of the obstruction. Congestion of the vessels with swelling and effusion into the substance of the mucous membrane of the duodenum will no doubt cause sufficient pressure on the common duct to obstruct the flow of bile, and may occasion dilatation of the ducts and of the gall bladder. A tumour outside the duct is not unfrequently the cause of temporary or permanent obstruction.

In some cases the obstruction of the duct has been discovered to depend upon the formation of hard fibroid material near the orifice. In a case reported by Dr. Sidney Phillips, "the stricture resulted from a tough fibrotic contraction of the outer wall of the duct." Three somewhat similar cases have been recorded by Dr. Moxon, Dr. George Johnson, and Mr. T. Holmes (meeting of the Clinical Society of London, October 28th, 1887, Report in "Brit. Med. Journ.", Nov. 5th, p. 995).

Obstruction of the gall duct is sometimes due to stricture resulting from very gradual contraction of the duct itself at one spot. Such cases are probably sometimes mistaken for impacted gall stones, tumours pressing on the duct, or tumours connected with the mucous membrane. The gall bladder is distended as in cases of obstructive jaundice, but there will be no colic or vomiting, and of course no history of previous attacks.

Obstruction to the flow of bile along the duct may be caused by adhesions, fibrous thickenings, and other changes outside it, or in the tissues in the immediate neighbourhood. Tumours in the neighbourhood of the duct of various kinds may indirectly compress or stretch the duct. Ulceration of the gall duct has been known to follow typhoid fever, and the pathological changes taking place subsequently in the seat of the ulcer and near it have led to such constriction as to cause complete obstruction and very severe jaundice.

Obstruction by Gall Stones.—At the time, or very soon after, a gall stone has become impacted in the duct there will be pain, perhaps not in one fixed spot, but over a rather wide area of the hepatic region. Oftentimes there is also the pain in the back and about the right shoulder similar to but more severe than that so very frequently experienced by those who suffer much from derangement of the liver, or from more serious disturbance affecting the organ.

The sudden impaction of a stone so large that it cannot pass freely along the duct is soon followed by serious and, at least to the patient and his friends, alarming symptoms. There is usually much stomach disturbance with very depressing nausea and generally vomiting frequently repeated and accompanied by feeling of the greatest distress and depression. The pain occurs in paroxysms so severe that the patient is perfectly helpless, is often doubled up and lies writhing in agony. The skin is pale, cold, and clammy, the pulse very small and quick, and often there are severe rigors and pallor of surface. The breath is cold, but the temperature, at least in many cases, is above the normal.

In cases in which concretions are firmly impacted in, and more especially when they are from time to time forced farther along, the duct, there is sometimes a very considerable amount of febrile disturbance which varies in intensity and may very easily be mistaken for a form of intermittent fever. Whether the febrile disturbance is in most cases in any way special seems doubtful. As is well known, the febrile state follows any considerable pressure or stretching of even the most passive tissues, and any irritating, not easily digestible, substances in the intestinal canal may excite a very high degree of fever. From the strikingly intermittent character of the febrile attacks, in some of the cases, Charcot has called the condition "Fièvre intermittente hépatique." He considers that pus or some septic substance formed in the bile afterwards passes into the blood and that thus the chills followed by the febrile state are caused. It seems probable, however, that the repeated stretching to which the coats of the affected duct is subjected would alone suffice to cause the febrile action without any septic disturbance. Several cases of the condition in question have been observed and recorded by Professor Osler, of McGill University, Montreal ("Medical Times and Gazette," July 30th, 1881). Cases in which the fever goes on for a considerable time often end fatally, death sometimes taking place suddenly as in severe remittent, sometimes after a longer period of time from blood-poisoning, exhaustion, and probably changes in the nerve centres.

Dilatation of the Ducts and Gall Bladder.—The degree of dilatation of the ducts in very prolonged obstruction, especially from impaction of a gall stone, is sometimes enormous, the dilated ducts in places exceeding an inch in diameter. When a section of the liver is made it will be observed in some cases that the united area of the sections of the ducts equals, or even exceeds, that of the intervening hepatic tissue. The dilatation is by no means uniform, as the tissue yields much more to the pressure in some places than in others. Here and there the walls of the dilated ducts are exceedingly thin, and sometimes they actually give way, allowing bile to extravasate into the spaces outside the ducts, from which small quantities from time to time make their way through

the attenuated walls of adjacent capillaries, thus leading to blood-poisoning by the admixture of the long stagnant and possibly decomposed biliary matter with the blood. In other places this gradual dilatation of the ducts results in alternate stretching and thickening of their walls, in consequence of which a beaded appearance results, and, indeed, generally there is great irregularity in the calibre. The mucous membrane is altered and the epithelial layer thickened and irregular, and otherwise changed. Sometimes the dilatation affects the vasa aberrantia and network of ducts in the portal canals.

The dilatation gradually extends backwards until the finest ducts and the tubes of the cell-containing network participate. These become distended, but after a time begin to waste, and many become gradually obliterated. The bile in many places gets into the interlobular and intercapillary spaces, causing wasting and stretching of the tubes of the cell-containing network, some of which are seen here and there extended across wide spaces containing clear fluid, and caused, no doubt, by the extravasation of bile which has been afterwards changed, and then in great part absorbed, serous fluid taking its place. The appearances seen in actual specimens I have obtained in this morbid condition can, I think, be explained only on the view that the liver-cells lie within tubes of delicate membrane.

In some cases, when the stone or constriction is situated in the common duct, the distension seems to be exerted in opposite directions,—towards the liver and towards the gall bladder. The size this viscus attains is sometimes enormous. In some cases, if the abdominal walls are thin, it can be felt, and often its lower limit may be ascertained by careful percussion. In these days relief can be easily afforded, and with very slight risk, by surgical interference.

Accumulation of bile in the gall bladder to a certain extent is not uncommon. The condition may give rise to chills or rigors followed by fever. The urine in such cases is generally high coloured and loaded with urates. There may be no actual jaundice, but the complexion will probably be sallow and the skin dusky under the eyes. The pulse will be quick and weak, and the patient will feel languid and probably drowsy. In short, the symptoms will be like those present in gall stones, but less pronounced. A sense of fulness, uneasiness, or actual pain will take the place of the excruciating suffering experienced in cases of obstruction or partial obstruction of the duct by a gall stone. Flatulence, discomfort about the stomach, with distension, and indigestion will perhaps be present. A smart purge, especially of calomel, will soon be followed by relief, with the escape of a considerable quantity of dark and perhaps acid bile.

Rarely is the gall bladder sufficiently distended to form an actual tumour that may be felt, and when this is so the swelling may perhaps

be situated at some distance from the usual position of the gall bladder. Dr. Young refers to a remarkable case, in which the gall bladder contained eight pounds of inspissated bile. ("Phil. Trans.," Vol. XXVII; Copeland's "Medical Dictionary.")

After bile has lain for some time in the gall bladder it undergoes important changes. Much of the contents is absorbed, and sometimes the viscus is occupied by a fluid which does not contain any of the constituents of bile. The mucous lining of the coats of the gall bladder and ducts sometimes suffer. Ulcerations in some cases may occur, and these may be followed by perforation and the escape of bile into the peritoneal cavity, peritonitis being caused, quickly followed by death.

Passage of Gall Stones.—The time occupied by the passage of a gall stone along branches into the common duct, and at last into the duodenum, varies much. Sometimes the process is very slow, extending over weeks, months, and even years, with many remissions and exacerbations of suffering, with attacks of jaundice again and again repeated. But, if the stone does not completely occupy the calibre of the duct, there may be no jaundice at all, scarcely any pain, and the stone may be voided in a few hours after the commencement of the attack. The suffering consequent upon the passage of a stone of considerable size, if continued and severe, may produce chronic derangement of the health and extreme emaciation. The patient is gradually worn out by the suffering and disappointment, and unless saved by surgical operation (p. 165), must die.

Nothing is more uncertain than the degree of suffering experienced in these cases. Sometimes a large stone causes comparatively little pain, while a small one, especially if it have sharp angles, may occasion the most acute suffering and cause complete collapse.

Very often the stone, large or small, is solitary, but sometimes the number of stones is enormous. More than two thousand small gall stones have been passed by one individual. A number may pass within a short time, or the process may be extended over many years. When the concretions are very small and numerous, they are spoken of as gravel, and may escape without occasioning any suffering. In such cases there may be occasional attacks of jaundice, lasting even for a considerable time. Great relief, and not unfrequently complete cure, may be effected by judicious washing out of the system, as is often effected by the Carlsbad and other waters.

After having passed from the gall bladder, gall stones may become encysted near the liver and remain perfectly quiescent for a number of years, or throughout life. In such a case, however, very slight causes may bring about stretching of the adventitious tissue around the stone, in which case inflammation will probably be set up, and will most likely

spread and cause general peritonitis, which will end fatally in a few hours.

Biliary calculi have been discharged through the umbilicus and other parts of the abdominal walls. Fistulous passages, often of considerable length, have been established, and, after pursuing a long and tortuous course, have opened upon some part of the surface or into the stomach, duodenum, or other part of the small intestine, colon, and even into the bladder and vagina. The formation of such passages is sometimes accompanied with severe suffering, but may be unattended by pain from first to last.

A gall stone may pass from the gall bladder into the cystic duct, remain there for a time, perhaps giving rise to violent attacks of pain, and then return again to the gall bladder. Stones which have traversed the common duct after exciting vomiting have been driven into the stomach, and have at last been rejected with food.

Calculi which have slowly passed along the duct and have at last reached the intestine have sometimes caused death by obstructing the bowel. Several cases are recorded in which the ilio-cæcal valve was the seat of the obstruction. Large stones sometimes pass from the gall bladder or a duct by fistulous communication into some part of the intestine. A small calculus has become impacted in the vermiform appendix, where it has set up inflammation, followed by abscess and death. In the "Pathological Transactions" for 1887, Dr. Pye Smith has reported a case in which a gall stone four inches in circumference, and weighing 270 grains, was felt by rectal examination in the ileum. Mr. Le Gros Clark refers to a case of intestinal obstruction by gall stones, which proved fatal by small calculi perforating the ileum ("Med. Chir. Trans.," 1871). The Transactions of the Pathological Society, says Dr. Pye Smith, "contain but few cases of obstruction caused by gall stones. The first was related in our first volume by the late Dr. Peacock; it occurred in a young woman of 27. The second calculus was shown by my father (Vol. V), and is now in the museum of Guy's Hospital (No. 1986[55]); the third by Mr. Potts, in 1864, Vol. V). My late colleague, Dr. Hilton Fagge, brought forward two cases, one in a woman of 56, and the other in a man of 64, both ending in recovery. Dr. Murchison, who collected twenty cases from all sources, showed one to this Society in 1869 (Vol. XX, p. 219); it caused fatal obstruction in an 'elderly female.' Two other cases were shown by Dr. Vanderbyl (Vol. VIII) and Dr. Baley (Vol. X). Dr. Ord showed the Society, in 1880, a large gall stone, which caused no obstruction, but diarrhœa (Vol. XXXI, p. 140). The remarkable calculus shown last session by Mr. E. H. Fenwick, was intestinal in origin, not biliary (Vol. XXXVII, p. 261). Frerichs had only seen two cases of obstruction of the bowels from gall stone. Mr. Treves, in his excellent monograph on intestinal obstruc-

tion, has collected sixteen."—("Trans. Path. Soc.," 1887, Vol. XXXVIII, p. 161.)

A very remarkable case of escape of gall stones after long circuitous passage came under my notice many years ago, in which several small gall stones, consisting of nearly pure cholesterine, escaped at intervals, and passed with the urine from the female bladder. The history of the patient left no doubt that these had by slow degrees made their way from the seat of their formation along fistulous passages behind the peritoneum, and eventually reached some part of the urinary tract. Several cases of the same kind are on record, in some of which the gall bladder, full of stones, seems to have emptied itself more directly into the urinary bladder, the stones passing along an extensive channel gradually formed, and through which bile in quantity was transmitted for some time before the escape of the gall stones occurred.

TREATMENT OF CASES OF GALL STONE.

Conditions tending to Prevent the Formation of Gall Stones.—While it is impossible to give a satisfactory explanation of the fact of the formation of gall stones in certain individuals, or to say why such concretions are not much more common than they are, it may be regarded as certain that the formation of gall stones is more likely in the case of those addicted to high living, in conjunction with sedentary habits, than in those who live sparingly and are active. In some families many members suffer from gall stones, and, as in the case of urinary calculi, an inherited predisposition seems to exist, though it certainly is less distinctly marked.

The fact of the occasional formation of gall stones in early life, and even in intra-uterine life, is alone sufficient to show that we are not yet fully acquainted with the precise conditions which favour and which prevent the formation of these bodies. At the same time, there is no doubt that those living under the hygienic conditions known to be favourable to growth and vigour are more likely to escape than those who get little air and exercise, live in hot rooms, and eat and drink freely; those who are active and abstemious than those who are sluggish and luxurious; those who are hard-working and industrious than those who are self-indulgent and idle. It is doubtful whether gall stones occur more frequently in stout persons than in those who are thin. They sometimes affect the most healthy-looking people, and are found at a time of life when the bodily functions are most actively performed. Nor do I think that persons who count themselves "bilious" are more frequently the victims of gall stone than those who are quite free from this troublesome and unpleasant train of symptoms. The so-called melancholic and phlegmatic temperaments are no doubt often associated with,

if not dependent upon, hepatic derangement or disease, but I doubt whether any increased tendency to gall stones exists.

In all cases in which there is a marked tendency to the formation of gall stones, or to congestion of the liver—when there is a sense of weight, fulness, or uneasiness in the right side, with or without the remarkable pain in the right shoulder—benefit almost invariably results from the frequent use of mild laxatives. While there is no doubt that our predecessors carried their views on these matters too far, it is, I think, certain that we err in an opposite direction, and sometimes patients are permitted to endure discomfort for many days, or even weeks, when a mild purgative occasionally given would bring relief. Probably many persons find this out, and experience no difficulty in obtaining the suitable, or, in not a few cases, it is to be feared, most unsuitable, remedies without having recourse to medical advice, or ascertaining the particular drug likely to be most useful.

Acidity, distension from flatulence affecting not only the stomach but the small and often the large intestine, occasional colicky pains, with frequent imperfect action of the bowels, or actual, and sometimes obstinate, constipation, often usher in and accompany an attack of gall stone, or partial obstruction from the presence of highly-concentrated bile. A slight purgative often affords complete relief, but it is sometimes necessary to give two or three doses, which may be followed by a free bilious evacuation, and complete relief of all the symptoms.

Of the value of frequent doses of taraxacum there can be little doubt, but generally the drug is given in doses too small to have much effect. Twenty grains of the extract or two or three teaspoonfuls of the succus taraxaci, twice or three times daily, for a week or two, may be given and the dose increased if necessary. Fifteen or twenty drops of the dilute hydrochloric acid and a little tincture of ginger added to the succus taraxaci in an ounce of water constitute a good addition. In some cases, however, when there is good reason to think that gall stones are already formed, or that the ducts are plugged with inspissated bile, carbonate or subcarbonate of soda should be added to the taraxacum in preference to an acid. The Taraxacum Coffee (Hooper & Co.) mixed with an equal proportion of ordinary coffee, seems really useful in many cases of constipation in which a tendency to gall stone is suspected.

An occasional dose of that old and highly effectual laxative castor oil affords relief sooner than more fashionable laxative remedies.

Liq. ammonii acetatis, potassii citras, and potassii acetas are remedies which I frequently prescribe in such cases with great benefit, but they must be given in sufficient doses and kept up for a fortnight or so at a time. Two drachms of the first, or half a drachm of the last, in

two ounces of water three or four times daily will be an appropriate dose.

Chlorate of potash, in doses of twenty grains three or four times daily, has been given, as well as the chloride of ammonium, in doses of ten or twenty grains in two ounces of water, but whether it answers better than the citrate or acetate of ammonia I am not sure.

The sulphates of soda and magnesia, or Carlsbad salts, are of great use in many cases. See p. 143.

Many comparatively new remedies have been recommended and largely used in the treatment of various hepatic disorders. Among the most important are podophyllin, extract of euonymin, and iridin. Lastly, there are various mercurials which, properly used, are among the most important. Small doses of calomel, blue pill, or mercury and chalk unquestionably do good in many forms of biliary derangement. One or two grains, or even less, repeated every other day, or once in three or four days for five or six doses, is often a very effectual mode of treatment, and I think it very likely that in some way or other mercurials really do make the bile to flow more freely along the ducts. Possibly, by causing the secretion to be formed in a more diluted state, or by some chemical action on the salts of the bile, mercury is beneficial. According to numerous observations mercurial preparations given to dogs actually reduce the quantity of bile secreted. Nevertheless, there is no doubt whatever of the highly beneficial action of mercurial preparations in hepatic affections of man. Care must be exercised in prescribing mercurials—too large doses must not be given, and the remedy must not be persisted in daily for many weeks at a time.

A person who has had one attack of gall stones should ever after be exceedingly careful as to diet. He should live most regularly, on simple diet, with only a very moderate allowance of meat and a little wine. He should endeavour to find out the mode of living which suits his health, and reduce the allowance of food to the amount just sufficient to keep him from losing in strength and weight. He should bear in mind the importance of liquid, the proportion of which to the solids taken should be considerable, not only because dilution makes solid food go farther and tends to keep matters to be eliminated in solution, but because there is evidence that in certain cases biliary calculi do exhibit evidence of being abraded or water-worn by the action of fluid, and though there is not, I fear, much chance of stones becoming so much smaller as to facilitate their escape, it does seem possible that sharp angles or points might be rounded off, and even soft stones or condensed biliary matter rendered softer. Moreover, there is reason to believe that inspissated bile, or portions of bile, locally highly concentrated, may give rise to all the symptons of gall stones. In such a case great benefit and even complete relief is likely to result from care that sufficient liquid is

taken, and there is no doubt that real advantage results from an occasional course of Carlsbad or other water.

In some cases the gall stones are so soft that they may be easily compressed between the finger and thumb, and it is conceivable that occasionally such stones may be gradually forced through the ducts by pressure of the bile accumulating behind. Frerichs seems to have concluded that gall stones might be dissolved by very alkaline bile. Undoubtedly, corrosive action results from the rubbing together of gall stones, while the growth and multiplication of bacteria in the interstices would set up chemical changes which result in the removal of small fragments and general corrosive action through the concretion.

Treatment of Pain from Gall Stones.—The extreme pain caused by the impaction of a gall stone in the duct is always much mitigated by warmth. The patient may have a warm bath, or hot fomentations, or poultices may be applied over the painful region. An india-rubber hot-water bottle is one of the best methods of applying warmth, and it may be got ready more quickly than anything else. Cold applications, such as a bladderful of ice, were recommended as long ago as 1826, by Briebeteau, but it is certain that very few sufferers in the present day would like the application or be relieved thereby. Opium or morphia should be given in these cases. If there is vomiting, the drug should be given by the rectum or hypodermically, instead of by the mouth. A grain of opium, or a third of a grain of morphia, may be ordered at first, and then half the quantity, or less, at intervals of two or three hours for three or four doses, when the violence of the pain will probably be relieved, and smaller doses at longer intervals will then be sufficient. In general it will be found that small doses, given at short intervals, will be more potent in bringing relief than larger ones at long intervals. Belladonna or opium may also be used externally. When the pain is excruciating, chloroform or ether inhalation may be adopted.

The old remedy proposed by Durande (1782), consisting of twenty to forty drops of sulphuric ether, and ten to twenty drops of spirits of turpentine, was widely advocated early in the century, but it frequently disagrees and often brings on vomiting. Further than the influence it has upon the stomach and duodenum, in exciting increased secretion and contraction of the muscular coats, it is doubtful whether it exerts any special action.

If the vomiting is distressing, iced soda-water, in very small quantities at a time, should be given. Hydrocyanic acid may be added, in the proportion of three minims of the acid hydrocyan. dilut. of the Pharmacopœia, to an ounce or more of soda-water or Salutaris water (distilled water with excess of carbonic acid), or effervescing citrate of magnesia, may be tried. But when vomiting is very severe it is worse than useless to allow the patient to be perpetually swallowing something. If a little

time is allowed to pass without the introduction of anything whatever, the irritable condition of the stomach is often allayed, and then one of the above fluids may be tentatively tried in very small quantities at a time, at intervals, the greatest care being taken not to give the fluid in greater quantities or faster than it can be absorbed. It is useless to attempt to give anything worthy of the name of food during the attack, but as the pain passes off a teaspoonful of iced beef-tea or milk may be given from time to time, the quantity to be gradually increased as the irritability of the stomach passes off. For some days, however, the patient should be allowed liquid food only, and in very moderate quantity at a time. When three or four days have passed without any recurrence of the painful symptoms, a little easily digestible solid food may be tried, such as sweetbread or good and well-cooked fish (whiting, sole, turbot), or tender chicken or game.

Surgical Operations for Gall Stones. Cholecystotomy.—Many cases of gall stones have been operated upon during the last few years and with excellent results. The operation is now generally sanctioned, and the risk is certainly not greater than that incurred in many surgical operations which are frequently performed. Some time since my friend, Mr. John Wood, removed a large stone from the gall-bladder of an old woman of seventy, who got well without a bad symptom. Probably Mr. Lawson Tait has had under his care a considerable proportion of the cases operated upon, and he states that up to 1885 he had performed the operation as many as sixteen times, with uniform success. His description of the operation as performed by him is as follows :—

"Having felt the position of the hepatic notch, I make an incision from the margin of the ribs over it directly, or almost directly, downwards, cutting carefully through the various textures until I reach the peritoneum. This is carefully seized by two pairs of forceps and pulled backwards, an opening having been made between the two pairs of forceps large enough to introduce my forefinger. With this I search for the gall bladder ; and sometimes I have experienced considerable difficulty in finding it. Generally speaking, the stones can be felt in the bladder before it is opened. In two cases out of the sixteen I have not found any gall stones ; in one case a mistake had been made, and in the other the disease was in all probability malignant. The details of these cases have already been published. Having found the gall bladder, I cautiously bring its fundus towards the wound and seize it by a pair of forceps. If it is distended, it is first of all tapped and emptied ; if it is not distended, or if it has been emptied, I lay it open by scissors or forceps to an extent sufficient to get a finger in ; the edges of the wound in it are then seized by forceps and any bleeding point secured. My finger then explores the bladder, and by means of forceps or scoop all the stones within reach are removed. A continuous suture is then

applied so as to accurately close the peritoneum by uniting the edges of the wound of the abdominal wall to the edges of the wound of the gall bladder, the two peritoneal surfaces being carefully adapted to each other. An india-rubber drainage-tube is then placed in the wound, and this is kept in for six or seven days, until it is possible to remove the stitches. If the stitches are removed along with the drainage-tube, the wound speedily heals; and, if all the stones have been removed, the patient is already cured. If the wound re-opens and bile discharges, or mucus from the gall bladder, the remaining stone which occludes the passage must be dealt with, either by crushing from the outside of the duct or in some other way as circumstances or the ingenuity of the operator may suggest. I certainly vouch for this, that so far as my cases have gone it is not known that they have any tendency to the reproduction of the gall stones. Certainly they have not given any indication of it so far. I would point out that, even if this did happen, an incision through the skin, probably only half an inch deep, over the site of the old scar, would reach the gall bladder without opening the peritoneum at all, and any re-accumulation of gall stones might be removed without the slightest difficulty or danger."—("The Surgical Treatment of Gall Stones," by Lawson Tait. The "Lancet," September 5th, 1885, p. 424.)

Like operations upon other organs in the abdomen, the number of successful operations on the liver and gall bladder have much increased of late years. With antiseptic precautions, and the greater care now exercised in details, the risk of many of the operations formerly regarded as not advisable has been so much reduced that it may be almost said, with respect to some, that they may now be included among the operations which should always be undertaken, unless some serious and exceptional objection on the ground of bad general health or constitution, or the existence of some other serious malady, forbids interference. Very recently (December, 1888), Mr. Knowsley Thornton reported to the Medical Society of London his last six consecutive operations, every one of which had done well. Among these were:—removal of the gall bladder, opening of the gall bladder, cutting into the liver for hydatids of the left lobe, perforation of the gall bladder, and abscess, in which more than one hundred stones were removed, some from the gall bladder, some from the surrounding abscess.

Two cases of cholecystotomy were brought before the Gynæcological Society by Mr. Stuart Nairne ("Lancet," March 31st, 1888, p. 616). Both did perfectly well, and Mr. Nairne advocates incision into the gall bladder in cases where, from obstruction of the duct, the viscus is distended. The operation in one of the cases is thus described:—"The gall bladder was pressed up hard against the abdominal parietes; and the only fear one had was that on the escape of the fluid

the gall bladder would fall away from the abdominal walls, and allow passage of blood or bile into the peritoneal cavity. This fear was practically groundless. The opening was made about the upper third of the tumour; a quantity of bile escaped; the edges of the incision into the bladder were retained by hooked forceps, and not by pressure forceps. The finger passed in detected stones, which were taken out with a small spoon. Three stitches were put in to retain the gall bladder in contact with the abdominal walls. As there was not the slightest suspicion that any extraneous fluid had escaped into the cavity of the abdomen, there was no attempt at sponging. An india-rubber drainage-tube was put in, and the wound dressed with iodoformed absorbent cotton. This patient, who was already reduced to a very low ebb, and was extremely emaciated, made an uninterrupted recovery; in fact, had neither shock or post-anæsthetic sickness, but felt so well in a few days that she desired and was allowed to get up."

Mr. Nairne further remarks:—"So far as my experience has gone, cases requiring cholecystotomy have appeared far more frequently in the female than in the male. Looking back over my general practice, I am satisfied there have been many cases which would not only have been benefited by, but now I think urgently demanded, incision of the gall bladder. I have myself, in the earlier part of my career, sat frequently with patients suffering from agonising pain, and administered chloroform and ether. Almost without exception these patients have been women. Indeed, thinking over the whole matter, and looking up my notes, I have been able to point to only two male patients who suffered probably from such a complaint. Of these two, one had a bad fit after drinking heavily for some time, and the other, a commercial traveller, was exposed to great irregularities in the matter of his diet. Both of these cases I now think were due to over-distension of the gall bladder, and might have been quickly, effectively, and safely relieved by incision. I think the risks attending this operation are very small. Altogether I have now incised the liver and gall bladder seven times, and have never had a death. But no doubt there are risks. The great risks are want of cleanliness in doing the operation, poking too much about the wound, and the presence of infectious or blood-contaminating sources. If these things are guarded against and the wound kept aseptic, I would not consider there was any more risk in an incision than there would be in administering ten grains of calomel."

In short, surgical intervention seems in many cases of gall stone to to have been fully justified by recent practice. The risk in opening the gall bladder, formerly supposed to be so very great, has proved to be not greater than that attending severe surgical operations. The protracted nature of many cases of gall stone, to say nothing of the terrible and repeated attacks of suffering and often very severe pain, would

justify surgical interference if attended with more uncertainty and risk than is really the case.

INFLAMMATION—ABSCESS—CIRRHOSIS.

The changes occurring in congestion of the liver have been already referred to in p. 137. It was there remarked that if the congested state of the capillaries persisted for some time it might be followed by further changes which would lead on to structural alterations in the hepatic tissue, which would render a return to the normal condition unlikely, and in some cases impossible.

The phenomena comprised in the inflammatory process may result in diverse pathological conditions, among which pus formation and abscess are the most acute, but cirrhosis is generally considered to be one of the most common results of inflammation of the liver.

Although in this part of my memoir I propose almost to restrict myself to the consideration of the essential nature of the pathological phenomena of cirrhosis, it will be necessary, in order to make the conclusions at which I have arrived clear to the reader, to allude briefly in the first place to some questions connected with inflammation, especially as it occurs in the liver. And, first, as to the starting-point of the pathological changes:—What is the nature of the first departure from the normal state, and in what way do the physiological phenomena give place to the morbid alterations, and how do the latter bring about structural changes which ensue?

As I long ago endeavoured to show, there is no sharp or abrupt line by which physiological or normal action is separated from pathological, morbid, or abnormal action, and in many cases it is the degree and not the nature of the action in which the departure from the normal state essentially consists. What may fairly be regarded as an exaggerated healthy action is unquestionably the change which constitutes the first step in many a pathological process. Notably is this the case in certain forms of inflammation. If only this first change can be recognized sufficiently early in its progress the inflammation may be stopped, and thus, perhaps, a very serious pathological process, resulting in the destruction of important tissues or organs, which can never return to the normal condition or be replaced by new ones, may be averted. Some consider that a nerve-change is the first in the order of occurrence, and in a sense this is correct, but evidence has been adduced which in my judgment clearly proves that the nerve change, like some other changes which accompany or succeed it, are but the consequence of phenomena which do not belong to the nerve category. These essentially consist in too rapid vital action on the part of the living matter of the textures implicated, and of the colourless corpuscles of

the blood. Besides, it is certain that all the essential phenomena of inflammation may occur in tissues destitute of nerves and vessels, and even in organisms which possess no nervous tissue whatever.

There is no doubt that inflammation of the liver and inflammation of the lung are characterised by the escape from the blood of certain substances which probably have for some time been accumulating in the circulating fluid. With these are perhaps a few red blood corpuscles. The blood which has extravasated soon undergoes coagulation, and after a time becomes the seat of disintegrating changes. The substances formed during these changes may at length be reabsorbed, in which case the tissue returns to its normal state without being in any way damaged. In the lung the air-cells are the seat of deposition of the substances which escape from the blood through the capillary wall, and when disintegrated the matter is soon reabsorbed; but in the case of the liver, the exuded matter for the most part occupies the spaces between the capillary walls and those of the cell-containing network. Its reabsorption would be less likely to occur quickly as the effusion had taken place amongst the structures of the organ, and their derangement, if not damage, would be more likely to ensue.

The so-called inflammation of the lung and the form of inflammation of the liver which may precede cirrhotic change are seldom associated with or followed by the formation of pus, and it will be well to consider whether in the present state of our knowledge this peculiarity can be explained. Both abscess of the lung and abscess of the liver are well-known diseases, but it is seldom that ordinary pneumonia is followed by pus formation, while "inflammation" of the liver, with considerable enlargement from the large amount of exudation poured out, almost invariably runs its course without the development of a single corpuscle. And in fact abscess of the liver is brought about in a manner very different from that of ordinary cirrhotic inflammation, and is usually met with in cases of a totally different kind.

"Inflammation," as its origin, course, and consequences are studied in hepatic and pulmonary tissue, is essentially different from inflammation as it occurs in the textures of the body generally. Not only may exudation occur to a greater extent, but the danger to life is due almost entirely to the extent of the tissue involved, rather than to the intensity of the process. Not only so, but in the case of the liver the "inflammation" leading on to cirrhosis almost invariably affects the entire organ, and so very rarely results in pus formation and breaking down of hepatic tissue as to render it doubtful whether the cases in which these extreme inflammatory changes occur should be regarded as belonging to the same category as the ordinary enlargement of the whole organ called hepatitis, and which may either result in cirrhosis or in a chronic enlargement which may slowly subside without the occurrence of

cirrhosis or other morbid condition, save thickening and some condensation of the capillary walls and those of the cell-containing network. The particular form of inflammation in the liver and lung referred to affects an area considerable in extent, as compared with the amount of tissue involved, for example, in a boil or in a small abscess consequent upon inflammation resulting from direct injury to a tissue.

In pus formation the inflammatory process reaches a stage far in advance of that reached by the pneumonic process in the solid lung of lobar pneumonia, or by inflammatory exudation in the substance of the enlarged inflamed liver.

But it is remarkable that in the formation of abscess in the liver there may not have been acute inflammation, and if in the early stages congestion of the vessels has occurred it will have passed off before the formation of the abscess commenced. As was observed many years ago, especially by my friend Dr. F. N. Macnamara (Calcutta, 1862), the liver just prior to suppuration is not highly congested, is not dark red, but pale in colour, and soft. There was "no congestion, no halo of redness." Especially in abscess associated with dysenteric ulceration does the early change appear to be more of the nature of a degeneration than an inflammation. At numerous points are to be seen small patches of pale, soft tissue, the paleness and softness gradually shading off into the surrounding hepatic tissue. The cells are found to be granular, many broken down and undergoing disintegration, and many oil-globules and *débris* are present. In the centre of the area of degeneration, says Macnamara, "we shall find the tissue liquescent or completely fluid, presenting to the eye the appearance of true pus, and here we have an abscess, yet no inflammation, and the puriform fluid may not present a single corpuscle to the most searching microscopical examination." After this breaking down in one or many patches there may be congestion in the neighbouring tissue, with increased action and pus formation, which begins not in the already softened tissue but in the congested area around it.

The gradual formation of an abscess in the liver probably takes place in this way:—Before the degenerative changes and softening had commenced it is probable, at least in some cases, that the capillaries have been congested even for a considerable period of time, and in some of them no doubt complete stagnation would have occurred. The stagnant blood would have undergone alteration, and its colouring matter absorbed or chemically changed and disintegrated, while at the same time many of the affected capillaries would waste and disappear. The liver-cells of the affected area being thus deprived of nutrient matter, and prevented from forming and discharging their secretion, would undergo degeneration. In fact, all the tissues of the affected area would be destroyed. If such changes as these occurred over the

greater part of the hepatic tissue, death would very soon result from blood-poisoning and exhaustion; but, if only a moderate area of tissue were the seat of change, many of the softened spots would run together, and a mass of soft degenerated tissue would result. At a short distance around this the vessels in the healthy tissue would be congested, and in this situation there would be increased action. The bioplasm of the adjacent tissues would grow in consequence of the free supply of nutrient matter, and very soon pus corpuscles would make their appearance, and would grow and multiply. As the pus corpuscles increased they would by degrees take up the disintegrated materials, if these had been preserved from decomposition, and a large abscess would soon be formed.

If the exact position of the abscess could be determined, and the contents evacuated before the abscess had become very large, and before the patient's strength had been much reduced by the illness, and a drainage-tube inserted, the cavity of the abscess would gradually contract, and be slowly obliterated, a little puckering of the surrounding tissue and a cicatrix marking its position. At length complete recovery would result.

As Regards the Formation of Pus Corpuscles.—In my work on Disease Germs, I long ago traced the formation of pus corpuscles from normal bioplasm of the blood and tissues, and endeavoured to show that in all cases of pus formation, the conditions were favourable to increased access of nutrient matter to the bioplasm. This increased nutrition and assimilation of nutrient matter on the part of the bioplasm, and the consequent rapid growth of the latter, is of the essence of the process. I was also led to conclude that, although some forms of bioplasm more readily gave origin to pus than others, pus might result from increased growth of the bioplasm of any tissue or organ in the body.

I also laid stress upon the remarkable change in the powers of bioplasm as the rate of its growth and multiplication increased, and the quite as striking loss of the special formative and individual constructive powers it possessed up to the time when an increased supply of nutrient matter was provided, and increased growth of the bioplasm commenced. Loss of formative power, gain in vital capacity, that is, in power of living and growing more quickly, and under widely varying conditions, are acquired as well as new powers of disintegrating and destroying tissues, and of appropriating the resulting products, which the bioplasm from which the pus bioplasm was derived did not possess.

There can be no doubt that in many instances, especially in the cases of persons residing in tropical climates, in consequence of over-work forced upon the organ by excessive as well as injudicious feeding, a condition is gradually established which at any time may very easily

and quickly result in the formation of abscess. Not only is the whole organ much enlarged, but it is excessively tender. If the patient persists in his free living, and continues to indulge his desire for very active exercise in hot sun, the chances of the occurrence of abscess are much increased. In such case the spleen is enlarged, sometimes very much enlarged, and it is often difficult to persuade the sufferers who have just returned from the tropics that prolonged rest is necessary for recovery. If persons in such a condition escape abscess, the first structural changes which are to end in chronic and fatal disease may commence. Rest, in its widest sense, is really what is required, not only rest for nerves and muscles, but stomach, intestinal, and liver rest. Small quantities of easily digestible liquid food—milk, farinaceous matters, and well-cooked fruit should be ordered—sufficient liquid being taken to keep the bowels gently acting. The patient should be allowed no alcohol whatever. If the bowels are constipated, an occasional dose of a solution of sulphate of soda and sulphate of magnesia will, by promoting escape of fluid from the bowels, relieve the congestion, and thus promote more free circulation in the hepatic vessels.

It is, however, far more common for abscess of the liver to be caused by the state of the blood itself. As was long ago shown by my predecessor in the chair of Medicine, in dysentery noxious matters are taken up by the blood from the ulcers, and these being carried to the liver are deposited there, and soon occasion changes which lead to the degeneration and softening of small areas of hepatic tissue, ending in the formation of abscess, as above described.

CIRRHOSIS OF THE LIVER.

Pathological Changes.—Although the condition known as cirrhosis is characterised by certain structural alterations of a very marked nature, the disease comprises a long series of changes, beginning with congestion of the capillary vessels, and resulting at last in the gradual wasting and degeneration, shrinking, and hardening, it may be of the whole of the hepatic tissue.

I shall, I think, be able to convince the reader that the tissue seen apparently between the lobules in advanced cases of cirrhosis, and usually regarded as fibrous or fibroid connective or cicatricial tissue—as neoplasm, adventitious, or new material—principally consists of the tissue of the lobules, and is only in part deposited or formed in the manner supposed. It is not strictly *interlobular*, for by far the greater part of it is really the altered tissue of the hepatic lobule itself, and in it the remains of the lobular secreting structure and the capillary vessels may be identified.

Instead of troubling the reader with a minute account of the several

respects in which my conclusions differ from those usually entertained and taught in these days, I shall venture to describe the structural changes which occur in this disease, as I have been able to demonstrate them in specimens, and I shall endeavour to explain the several stages through which the healthy liver passes until it slowly arrives at the condition of the small, hard, contracted liver of cirrhosis, and to establish certain broad principles as regards the nature of the disease. As in the case of other tissues and organs of the body, the phenomena included under the term "inflammation" play an important *rôle* in hepatic pathology; but, at the same time, observation has led me to conclude that some of the most important changes usually regarded as resulting from inflammation, and spoken of as inflammatory, are not really of this nature, and I shall endeavour to show that ordinary cirrhosis of the liver, so far from being a consequence of inflammatory change, is really due to an altogether different series of pathological phenomena. In the first instance, there is no doubt engorgement of the capillaries of the lobule with slowing of the blood-flow, and in many cases this state of things persists for a considerable time. The distension of the portal vessels with an undue proportion of blood is sufficient to cause that increase in size of the liver which is frequent in the early stage of the disease. The hepatic enlargement is often so considerable that it can be easily detected by palpation. In some persons this enlargement occurs frequently, improvement taking place and the congested state passing off if only time is allowed for such beneficial change. If, however, the introduction of food and fluid into the intestines in undue quantity is persisted in with little or, as too often happens, without any intermission, the accumulation of blood must continue, and the pressure exerted upon the secreting structure of the liver must be maintained. Increasing in severity, the pressure and the interstitial effusion, which after a time occurs, derange the action of the cells, which at length are damaged, and permanent structural change must soon follow.

In the healthy condition, whenever an unusually large amount of blood is suddenly carried to the liver, the pressure is prevented, or very soon relieved, by much of the blood being diverted into the splenic vein. The spleen, being a dilatable reservoir, acts the part of a safety-valve, and all danger to the hepatic structure passes away. Slowly as the blood already in the organ is depurated, more blood takes its place, and so on, until all has passed into the hepatic capillaries. After resting for a few hours the liver is again ready for work, and the recently absorbed substances from the next meal come under the influence of the hepatic cells.

If, however, the congested state of the hepatic vessels has persisted for a considerable time, or when many successive attacks of congestion have recurred at short intervals over a period extending perhaps to

many years, exudation of serum with various imperfectly altered matters in solution and leucocytes will have taken place. This exudation collects outside the capillaries, principally in those interstices or spaces which exist between the capillaries and the tubes of the cell-containing network. The leucocytes, the bioplasts of the capillary walls, and those of the hepatic cells, will increase in size and then in number by division. The liver will now be considerably enlarged, and the increased size may persist without much alteration for weeks or months. Slowly the leucocytes, as well as the small particles of living matter in the lymph, having grown and multiplied, give rise to a certain amount of transparent coagulated matter allied to fibrin which undergoes change and condensation, at last taking the form of what has been termed "cicatricial tissue." The amount and the importance of this cicatricial tissue have been from the earliest days of investigation up to and during the present time greatly exaggerated, and I venture to think that this substance at the utmost plays a very subordinate part in the pathological phenomena of cirrhosis.

All the essential changes observed in the cirrhose livers I have examined might certainly have proceeded, and the same morbid structural results have been brought about, in the entire absence of such adventitious tissue, and of the inflammatory changes supposed to be connected with it. In fact, I think a healthy liver might pass through all the stages of the disease and advance to extreme cirrhosis without having been inflamed, without the formation of cicatricial tissue, without any of that contraction and constriction supposed to be of the very essence of the disease.

Possibility of Recovery from the Cirrhosed State.—Looking at a liver in an advanced stage of cirrhosis, and contemplating the gradual changes which have steadily proceeded from the very beginning of pathological action, one would be led to conclude that all hope of recovery—of return to the normal condition—disappeared from the first. This idea is sanctioned and supported by what we have been taught concerning the nature of the disease. The gradual increase and steady contraction of firm adventitious fibroid tissue, gripping more and more tightly the gland structure, causing first its atrophy, then its disintegration and removal, seem to be the component elements of the theory of cirrhosis which has been widely accepted without opposition by physicians. And yet careful inquiry into actual cases of the disease will convince us not only that now and then recovery does take place, but that the rate of the progress of the malady varies extremely, and is in some instances so very slow that it can scarcely be said to shorten life. And although the patient cannot be considered to be in a state at all approaching the healthy condition, he may, nevertheless, be able to discharge his ordinary work, and even enjoy life.

From careful study in the post-mortem room, we learn that different parts of the liver in cirrhosis suffer in very different degrees, and in cases in which death has resulted from some other malady or from accident before the disease has reached an advanced stage, we are often struck with the considerable amount of healthy and active gland tissue which remains almost intact, although here and there cirrhotic change has completed the destruction of the secreting tissue of many of the lobules. When cirrhosis occurs in the young, or possibly in persons who have not advanced much beyond middle age, there is reason to think that here and there new secreting structure may be formed not far away from spots where many lobules have been completely obliterated by disease. While thus some cases run their course to death in a short time, others pass through the several stages of the disease very slowly, and there is no doubt that by good management the progress of cirrhosis may be retarded and rendered very slow, if indeed the disease cannot be completely checked; and the work required of the liver would be discharged by the comparatively small amount of hepatic tissue yet retaining its healthy condition. This good result can only be gained in the case of those who submit to live upon very small quantities of food. Such persons must be made to understand that they have but comparatively little hepatic tissue left to do the work of their body, and if they would live they must be careful not to risk overworking the little liver texture that remains in a healthy or partially healthy condition.

Question of Enlargement preceding Cirrhosis.—It is undoubtedly true that in many cases the contraction of the liver is preceded by enlargement, and that in some cases the organ is enormously enlarged. But this increase in size is not a necessity, and contraction may proceed to an extreme degree although the organ has never increased in size at all. Many cases have been recorded of cirrhosis in young people and in children, the contracting process having steadily gone on until death occurred. Several instances have come under my own notice which seemed to be true cases of contracted liver at different ages and from different causes, in which there had never been evidence of any inflammation. As far as could be made out there had never been enlargement, and in many of these cases the disease could not be attributed to irregularity in living, to excess of food, to alcohol, or to any special hygienic circumstances. Dr. Nelson Jones, of the Swansea Hospital, sent me in 1885 notes of a case of cirrhosis of the liver, with ascites, in a boy of 19. There was no history of alcohol, syphilis, or of any mismanagement likely to produce the disease. It is true the boy was a miner working underground, but it has not been shown that mining is one of the causes of cirrhosis in the young. In this case, however, "The liver was enormously enlarged, and you could hardly place a

sixpence on its surface which was smooth, there being irregular knobs all over, some as large as walnuts."

In a case of cirrhosis in a child, the organ had gradually diminished in size without there having been any previous enlargement whatever. Several cases of cirrhosis occurring quite early in life have been observed and recorded.

As far as I am able to judge, neither enlargement nor inflammation is a cause or invariable accompaniment of the cirrhotic state, and it would seem that cirrhosis may run its course without being preceded by any increased action. Cirrhosis seems to be essentially a wasting, a degeneration, with shrinking frequently of all the structures of the lobule, but in some cases the branches of the artery are actually larger than in health. The disease may probably be caused in many ways, and may be complicated and preceded and accompanied by other pathological changes. Degeneration and wasting of the liver may happen at any period of life. The change may begin even before the development of the organ is complete. Owing entirely to developmental faults or defects, the liver of the fœtus *in utero* may be cirrhosed, and young children occasionally die of the disease. This condition often occurs in adolescence, but, as is well known, it is most common in middle life, and from this period to old age.

Hypertrophic Biliary Cirrhosis.—In the disease which has been called hypertrophic or biliary cirrhosis there is often considerable enlargement of the whole organ, with excessive derangement, which often comes on almost without warning, perhaps after a course of reckless over-eating and drinking. The veins and capillaries are distended with blood, and the cells are gorged with biliary matters which they cannot get rid of fast enough. The whole organ may be much enlarged, and as it were clogged with matters that should be excreted. The blood is surcharged with excrementitious matters, and there is great and often immediate danger to life, and especially in cases in which, as often happens, the kidneys are also involved. In many cases the pathological condition is almost acute. A man having for some time indulged in irregular living, and especially in excess of nitrogenous food and alcohol, is taken suddenly ill with vomiting and perhaps diarrhœa. Sallowness, and often actual jaundice, is observed, and not unfrequently the mind is clouded from the outset, and the patient may soon become delirious. There is tenderness over the hepatic region, and generally the hepatic dulness will be found to extend an inch higher and lower than the normal limit. Before the patient has been laid up for many weeks there may be a serious attack of hæmorrhage from the capillaries of the mucous membrane of the stomach and bowels. Blood, even to the amount of pints, and due entirely to capillary oozing, may be rejected by vomiting and passed by the bowel

If the hæmorrhage does not destroy life in the course of a few hours, and in the great majority of cases under the age of forty it is not immediately fatal, the hepatic congestion may be relieved for a time, and then return perhaps in an aggravated form if care is not taken to prevent it, the liver doing little or no work. Ascites with some anasarca soon follows, and oftentimes quickly increases so that relief has to be sought by tapping within a short time after the commencement of the hepatic disease. The case may terminate quickly by attacks of hæmorrhage, or by blood-poisoning, or slowly, that is in the course of two or three years, by chronic contraction of the liver, and the consequent changes in the blood, general debility, disturbed digestion, exhaustion, and if the patient lives for a considerable time extreme emaciation.

In this form of cirrhosis degenerative changes in the cells at the periphery of the lobules proceed apace, and in cases in which death has occurred within a few days or weeks of the apparent commencement of the illness one is often surprised at the extent of the morbid change. The outer third of the thickness of the lobule may be the seat of wasted and contracted tubules and cell-destruction. According to the views of several eminent pathologists, this form of cirrhosis commences in inflammation of the coats of the ducts, which spreads thence into the lobules of the liver (see page 188). The principal changes have been regarded as intralobular, as distinguished from the ordinary form of the disease, which is said to be due to perilobular or interlobular inflammatory action. Whether the facts at present known justify us in accepting this as a general proposition is, I think, doubtful. It seems to me that the two supposed different forms of cirrhosis are very closely allied, and differ more from one another in the rate at which the morbid changes proceed in the early stages than as regards the nature of these changes themselves. But the exact morbid alterations will be considered later on.

Causes of Cirrhosis.—Cirrhosis may occur without any definite exciting cause that can be discovered. It may result from chronic bad living and occasional starvation, irregularity as regards the amount of food in a given time, from luxurious living and excessive feeding, or it may be brought about by the ordinary structural changes in the liver which occur in the organ as old age advances, and which are observed in some individuals even as early as forty. But probably the most common of all the causes of cirrhosis is excess of stimulants, while a very certain method of inducing the disease at an early age is the system of swallowing small quantities of diluted or ardent spirits at short intervals and without food being taken. This system of self-destruction is much indulged in by many who work in markets and have to be up very early in all weathers, making bargains and effecting

sales which cannot be satisfactorily completed unless both parties to the bargain yield to the pernicious fashion of having a drink. A large percentage of those who live in this way die of cirrhosis of the liver, often accompanied by renal disease, before they reach the age of fifty, many looking old and worn-out before they are forty.

While it is true that many cases of cirrhosis cannot be traced to alcoholic irregularities, it is certain that the majority are indirectly thus occasioned. The alcohol does not cause the disease by any direct action upon the hepatic tissue, as is often taught, but in a very indirect manner, probably, by inducing by very slow degrees and over a long period of time alterations in the blood whereby it becomes unfitted for nutrition, while various matters which ought to be excreted continue to accumulate. At length the action and nutrition of every tissue and organ in the body are deranged. We must, however, bear in mind that there are instances of inveterate wine and spirit drinkers who have over-indulged for fifty years and have not suffered in any way, but such fact no more proves that the general conclusion is wrong as applied to the great majority, than the fact that here and there a man consumes two pounds of meat daily without suffering, proves that most of us might live in the same manner with impunity. There seems to be a small percentage of persons among us having exceptional organs who can do and can bear without penalty more than the majority. Just as there are men having brains of marvellous powers, and musculo-nervous apparatus of capacity and endurance hardly credible, so we find a few individuals blessed or cursed with digestive organs capable of working with an intensity and frequency and for a length of time that are surprising when measured with the eating capacity and digesting power of the general average.

Developmental Defects as a Cause of Disease.—The influence of developmental defects and faults in the causation of failure of action of important organs, and premature degeneration and decay, is probably much greater than is generally supposed. Many cases of disease of important glands, as well as cases of failure of the brain, spinal cord, and other parts of the nervous system, are due to this circumstance. Of all forms of hepatic disease, the most serious and rapidly fatal is, I believe, due to congenital defects. In this disease the liver seems to work well up to a certain time, and then to fail utterly. In two of these cases which I have carefully examined, I found that in the central part of each lobule there was an absence of liver-cells, a few granules and oil-globules being all that remained. It would, therefore, seem probable that new cells had been formed, and had passed towards the circumferential part of the lobule only up to a certain period of life. As there were no new cells or nuclei in the centre of the lobule to replace those which had reached maturity and active secreting power, a time must

come when all working power would fail. The following, as it seems to me, is the probable explanation of those cases of acute jaundice, with destruction of hepatic secreting structure, and of some other cases in which an important organ suddenly fails from degeneration :—In consequence of imperfect development of certain structures dependent perhaps upon impaired developmental power of the bioplasm which produced them, and irregularity in the changes occurring during the formation of tissue, the structure when formed is weak and not lasting. It works for a time, and then utterly breaks down. Certain forms of bioplasm deteriorate, or wear out as regards productiveness before their time, and consequently at a certain period of life the reproduction of cells or elementary parts ceases, and the organ fails to act. In the case of the liver and some other organs this means death.

It is probable that many pathological changes occurring at various periods of life, from very early infancy to old age, are really due to developmental faults and failures. Almost every one has a weak point, a tissue easily deranged, an organ that acts imperfectly, and the action of which is frequently disturbed. It is seldom indeed that one meets with an individual who is in all respects well developed and all of whose tissues are equally strong and active, and able without suffering to bear strain. Of those who distinguish themselves in competition, nay of those who beat the record, how few there are who do not suffer in consequence. The early strain initiates or favours changes which result in damage at a later period, so that tissues and organs unexpectedly succumb at a time of life when they ought to be perfectly healthy and capable of active work.

Shrinking and wasting with deterioration or loss of function of the tissue affected are processes which occur in health as well as in disease. Indeed, the actual lesions may differ little as regards their essential nature. It is the period of life at which they occur that is the important point. A degeneration at 20 or 30, at least in the case of some tissues and organs, may be of little moment, as the place of the wasted tissue may be taken up by new, but at 60 or 70 the formation of new structure is no longer probable. Again, shrinking and wasting occurring in secreting organs may cause one man to be as old at 50 as another is at 70; while in a few rare instances so well developed are all the tissues and organs that all get old together, and failure is so gradual that it is impossible to say which first fails. On the other hand, even in the young, nay, occasionally almost as soon as the tissue is formed, it may begin to deteriorate and waste. Whenever this premature wasting takes place there will be loss of bulk in the working tissue, while the growth and formation of the weak and evanescent texture are often associated with enormous increase in bulk. The residual passive connective tissue, however, which may result in the course of the

degenerative process, occupies very little space as compared with that taken up by the healthy texture during its period of functional activity.

In a given case, whether the premature wasting and decay are due to some developmental imperfection, to lack of developmental power, or to the tissues, although well formed, having for a time lived too fast, may be open to question. In some cases all these circumstances may have contributed to the result. Generally, lack of enduring power as regards tissues and organs is undoubtedly due to too rapid development. So quick has been the formation of tissue, that there has not been time enough to allow of its consolidation and firmness, without which there can be little endurance and power of resistance. If imperfectly or too quickly developed tissue be subjected to undue work or sudden strain or shock, decline of power will result, and premature decay and degeneration will soon follow. In some cases, therefore, it is obvious that premature decay is preventible, while in others it depends upon vital conditions or peculiarities so deep as it were in the organization, and often hereditarily transmitted, that it is not to be prevented by any means that have yet been discovered.

Shrinking and wasting at an early age will be serious or of comparatively little consequence according to the particular tissue or organ involved and to the amount of tissue affected by the change. There may be wasting and degeneration of a nerve, or a portion of a nerve centre, of a muscle, a set of muscles, or of all the important tissues of a limb, partial degeneration of an organ to be compensated for by increased healthy growth in another part, or wasting of an organ necessary to life, as of an important part of the brain, medulla or spinal cord, soon causing results disastrous to the organism or leading to early death.

Of the minute Changes in Cirrhosis.—The Cirrhosis of our text-books, and indeed of all the authorities known to me, is said to be due to inflammation, to hyperplasia of the interlobular connective tissue of the liver, to the formation of a new fibroid or connective tissue, followed by cicatricial contraction. As I have already endeavoured to prove, the interstitial connective tissue as a necessary supporting framework exists not. During the early growth of all livers, even at a time when the organ is active, and in the liver of small animals, such a tissue is not to be demonstrated even when the liver has attained full development and has long been in active work. When such tissue is present it is but a passive substance, useless or an encumbrance, a disadvantage to the gland, rather than as has been affirmed a useful texture giving support to the delicate gland elements and vessels. Any hyperplasia which may occur near such tissue, or which may involve it, results from changes in which such passive tissue itself takes no active part.

Moreover, I must remark that microscopical appearances, generally

relied upon as indicating fibroid change and as causing subsequent contraction and strangling of important textures, are often fallacious. If the same preparation in which such tissue is supposed to be demonstrated be examined according to principles known to be advantageous for rendering evident certain definite structural elements, a wholly different conclusion would be drawn, and new facts suggestive of a very different interpretation of the pathological changes would be presented to the mind of the observer. In the ordinary accepted theory of cirrhotic change we have, I think, an example of superposed pathological conjectures built up by successive authorities whose respect for tradition prevented careful examination of the views handed down.

We have been assured that in cirrhosis the liver is enlarged in consequence of having been infiltrated with "a soft vascular connective tissue rich in young cells"—that the organ is everywhere "infiltrated with young cells which are converted into connective tissue"—that it is overrun with connective tissue by the growth and contraction of which its vessels and ducts and other tissues become compressed and at length completely obliterated. Regarding the matter from the point of view established by actual observation, the more this accepted doctrine is considered the more will it seem to be based upon a purely artificial conception of the pathological processes at work. It is indeed very doubtful whether any one of the phenomena above referred to is really necessary to cirrhotic change. Certainly cirrhosis may run its course without infiltration with young cells, and without the liver being overrun with connective tissue. Neither is contraction of connective tissue, or of any other tissue, necessary for the obliteration of vessels, ducts, and other structures in the liver or elsewhere. As far as I have been able to ascertain, there is really very little to warrant the above conclusions, and, as already remarked, it is pretty certain that the appearances supposed to justify them are more dependent upon the method adopted to prepare the specimens for microscopical examination than upon the actual structural changes which have occurred. Of this fact any one may convince himself if he will only take two thin sections of the same cirrhosed liver, and prepare one so that it can be mounted in Canada balsam, and soak the other for some time in syrup of glycerine, and examine it by the same magnifying power, which should be one of two hundred diameters or more.

The careful study of the minute changes upon which the shrinking and wasting process as it affects the tissue of the liver in ordinary cirrhosis depends is of the greatest interest. Indeed, these changes which at last result in the destruction of the organ itself, and the reduction of the organism to a condition such as would be brought about if the liver had been extirpated, may almost be regarded as the result of a natural experiment which could only be successfully carried out in a very

gradual manner by natural processes. Here we have, I think, an example of the very slow extirpation by a natural process of one of the largest and most important glandular organs in the body—an organ absolutely necessary to life, the free action of which is of special consequence during the early and highly active period of existence. During the gradual deterioration and extinction of the hepatic function which results from cirrhosis, the organism gradually accommodates itself to the altered conditions under which physiological work must be carried on. Individuals may live for some considerable time practically without an organ, the sudden cessation of the action of which for only a very limited period, when the body was in a state of vigour and free healthy action was proceeding, would be surely and almost immediately fatal.

In examining a thin section of several lobules of a healthy human liver, one is struck by the proximity of each to its neighbours. In fact it is only here and there that interlobular spaces or intervals are observed, in which lie the branches of vessels and ducts which are connected with the adjacent lobules, while at many points of the circumference of each lobule the capillaries of adjacent lobules are directly continuous. In a cirrhosed liver, on the other hand, each lobule seems to be almost isolated, to be separated from its neighbours by a layer of tissue of considerable thickness, and which differs entirely in appearance from the proper tissue of the lobule, exhibiting, when examined in the recent state, the opacity of fibrous tissue, a change causing it to contrast remarkably with the transparent character of a thin section of healthy liver. As the disease advances the lobular tissue seems to diminish, and the apparently intervening texture, which is supposed to be an exaggeration of the connective tissue supposed to be a necessary structural element—in fact, the so-called Glisson's capsule—increases in extent. If the cirrhotic change has been proceeding only for a short time, there will be only what has been described as a thin layer of this hardened tissue corresponding to the circumferential part of the lobule. But in it will be seen irregular networks of tubes containing cells which are continuous with, and indeed are the circumferential part of, the tubes of the cell-containing network irregularly thickened, contracted, and otherwise altered by disease. The reticulated arrangement is very distinct, and the divisions and ramifications are easily traced by the small cells they contain, and which may be tinted with a solution of carmine in ammonia, by which means every single cell and nucleus may be distinguished.

In well-prepared specimens many of the tubes of the network in question can be shown to be continuous in the other direction with very narrow ducts or with the interlobular network of very fine ducts. This very important fact has been placed beyond question by careful

injection of the ducts in livers not very far advanced in the cirrhotic state, not only in the case of man, but in some of the lower animals. I have already referred to a network of fine ducts between the terminal branches of the latter and the most superficial portion of the tubes of the cell-containing network of the lobule. See Figs. 59, 60, Pl. XIX. The extent of this network varies in different cases, and the conclusion is almost forced upon the mind that in some instances the part of the ductal network nearest the lobule may be occupied with cells at one time and destitute of cells at another. At one time the secreting cells grow large and increase in number; at another they become reduced in size and number, and in some places disappear. In fact when the work of the liver is very active the secreting cells extend into the tubes, and these tubes then become the outer part of the cell-containing network; while, if the work of the liver is reduced, the cells shrink, leaving many of the tubes free, in which case this part of the network would be regarded as ductal. In some of the lower animals, under varying circumstances as regards the quantity of food within the limits of health, considerable changes may be observed in this ductal network. In the pig, it is probable that when the animal is very freely supplied with food the hepatic cells extend into this interlobular ductal network; while in an opposite state of things the hepatic cells, becoming reduced in size and number, and the network of fine ducts, destitute of cells but containing oil-globules and granular matter, would increase in extent. See Figs. 59, 60, Pl. XIX, page 114. Although remaining pervious, many of the tubes of this network may become so narrow as to be scarcely perceptible, or imperceptible unless the examination is conducted in a special manner, and the tubes have been rendered evident by injection with a transparent injecting fluid. In old and partly shrunken livers, this network is more extensive than in young and active organs. In cirrhosis that has existed for some time, many of the tubes of this network will be found to have become impervious, and not a few will have completely disappeared; a sufficient number, however, remain open to carry off the reduced quantity of secretion.

Many of the elongated tubes with small cells in their interior, seen in contracted livers, are of greater length, without having lateral branches, than any that I have been able to demonstrate in the network in health, and some are much wider, having two or three rows of cells within them. Of the elongated tubes, some, the largest probably, I think belong to those ducts which extend into the lobule to join portions of the cell-containing network some distance from the surface; others are, no doubt, ducts which have remained pervious while the lateral branches have wasted, and have been instrumental in carrying away a small quantity of bile found for some time after the degenerative process had commenced; a few of the more twisted are probably ducts

along which the bile continued to pass after numbers of the lateral branches had wasted and had altogether disappeared.

As the disease advances, many of the lobules which have degenerated together, perhaps in collections of half a dozen or more, which have ceased to undergo further change, save very slow contraction and condensation, form a small mass of contracted hepatic tissue. Around and between many such collections will be altered vessels of the larger portal canals. The lobules adjacent to these vessels will have undergone contraction greater in degree than that affecting lobules situated at a distance. The alterations just referred to give rise to puckerings and irregularities throughout the hepatic tissue, and on the surface such irregularities will be very strongly marked, and the surface will be very uneven in consequence. But the irregularities arise not from inflammation of the extensions of Glisson's capsule into the substance of the liver, as is generally supposed.

At the same time that the cells in the peripheral part of the lobular tubular network have been shrinking, the ductal portion of the network has been undergoing change. Many of the finer tubes, remaining for a considerable time empty, contract, and gradually waste. As the amount of bile formed becomes less and less, many of the tubes which formerly carried the secretion to the ducts, being no longer required, shrivel, and ultimately disappear. The cells seen in many of the more elongated ductal tubes exhibit appearances which render it probable that they have descended from the cells which lined the ducts, rather than from the hepatic cells of the cell-containing network which are concerned in the secretion of the biliary matter.

Advanced Cirrhosis.—When the cirrhosed state is more advanced, what was once a lobule will be found to occupy considerably less space than in the normal state, and to consist of an extensive area of degenerated tissue with a small collection of hepatic cells, in the central part only. This central part alone retains the character of the original lobule, Fig. 74, Pl. XXI. The outer part of these cells is granular and more opaque, and their shape is less regular than that of the healthy cells. Oil-globules may be seen, but biliary particles are not usually found in them. By the time this phase of the disease has been reached in a lobule, all capacity of discharging function has been lost, and what was once the lobule is now but the altered and degenerated remains of the original and formerly active structural elements. If, however, a little secretion were formed by the few remaining cells in the centre of the lobule, it would scarcely traverse the few very narrow irregular channels which remain.

Although anything approaching the solid capillary network of the lobule has long disappeared, many of the capillaries still remain pervious, and a very reduced quantity of blood finds its way from the interlobular

CHANGES IN CIRRHOSIS.

Fig. 74.

Cirrhosed liver showing the wasted tubes of the cell containing network of the outer parts of the lobules with the cells of the central parts of the lobules only remaining. × 20. p. 184.

Fig. 75.

Cell containing network, near the centre of the lobule. Human liver. The capillaries were dilated to twice their normal diameter, as represented in Fig. 79, Pl. XXIII. × 215. p. 76.

Fig. 76.

A portion of the degenerated tubular network seen in Fig. 74, more highly magnified. Small condensed liver cells are seen in every part of the specimen. × 215. p. 185.

Fig. 77.

A portion of the cell containing and ductal portion of the network nearer the inter-lobular fissure than Fig. 76. Several of the elongated tubes referred to in p. 103, are shown. × 215. p. 185.

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branches of the portal vein to the intralobular venule. At length, the few cells remaining in the central part of the lobule undergo further degeneration, and at last disappear. What was originally a lobule, active in every part and concerned in the production and removal of highly complex and very important chemical compounds, is represented by a smaller mass of fine fibrous-like tissue, in which not a cell can be discerned like the healthy liver-cell, and which occupies less than half the space taken up by the lobule in its healthy condition. But in every part of this degenerated mass, which has often been described as connective or fibroid tissue, are to be found the remains of anatomical elements which incontestably demonstrate it to be not adventitious tissue deposited in the interlobular spaces, but the actual tissue of the lobule itself altered. Everywhere traces, and more than traces, of the cell-containing network with some cells remain, exhibiting a reticulated arrangement more distinct than in health by reason of the great narrowing of the tubes and condensation of their walls, and the wasting of the intervening capillaries. See Figs. 76, 77, Pl. XXII. These illustrations should be carefully examined and compared with other drawings, especially Fig. 68, Pl. XX, and Figs. 42, 43, 47, 51, 59. Any difference in the magnifying power should be carefully noted in instituting a comparison. Any one who has carefully examined such specimens from a liver which has not yet reached the extreme stage of the disease will, I am sure, feel convinced that the cells of the liver were situated in a network of tubes alternating with the capillary network.

Whenever the changes above described have affected a number of lobules near to one another, there will be a collapse or falling in or shrinking, as compared with collections of lobules which yet remain intact, or in which the degenerative changes have not advanced in any considerable degree. The alteration in volume here and there will necessarily give rise to some irregularity and puckering of the adjacent hepatic structure. The irregularities seen upon the surface, remarkably developed in what has been fantastically termed the "hobnail liver," and extending in a more or less distinctly developed form to every part of the liver in advanced cases, are due to passive changes only—to wasting, shrinking, and degeneration of element after element, structure after structure—and not to the exercise of pressure or constriction by fibrous or cicatricial tissue resulting from changes in lymph poured out from the blood in the course of inflammatory action. Degeneration following and consequent upon overwork has more to do with cirrhotic change than inflammation and contraction of effused products.

In some cases of cirrhosis the liver-cells soon become very small, while the walls of the tubes of the cell-containing network are found to be irregular and exceptionally dense. They can consequently be made out with the greatest distinctness, and sometimes at a period of the

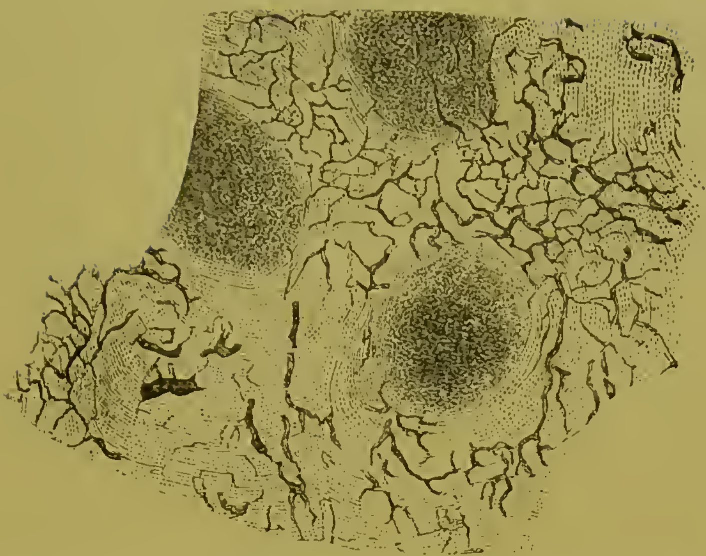
disease when degeneration has not proceeded to any great extent. In such cases the view concerning the structure of the liver deduced from a consideration of the pathological alterations will be in accord with, and will be confirmatory of, that based upon the appearances demonstrated in the healthy liver, the ducts of which have been successfully injected and prepared according to the principles I have advocated in "The Microscope in Medicine" and in "How to Work with the Microscope," as well as in the present work. See page 208. In cirrhosed livers one can obtain specimens which exhibit the transition from the normal tubes of the cell-containing network with walls so thin they can only be demonstrated in injected preparations, to bodies which are so far removed from the tubes of the ordinary cell-containing network as to closely resemble "connective tissue corpuscles." The shrinking, wasting, and condensation affect the lobules generally in cases in which the disease has been going on for some years. Many lobules are completely obliterated, and the entire liver, consisting of lobular remains and the *débris* of lobules, may be reduced in weight to a few ounces. A hardened mass of inactive tissue destitute of function being all that remains of an unceasingly active organ, having a highly elaborate structure, and which weighed perhaps four pounds in its healthy state.

It is true that the rate at which pathological change proceeds in cirrhosis varies greatly in different cases, and also that the part contributed to the result by the process usually termed inflammatory, is in some cases considerable, in others inappreciable. No doubt in certain examples of obstruction to the onward flow of bile, whether in the liver itself or in the large ducts outside, comparatively sudden and unimportant inflammatory changes with exudation result; but my own observations do not permit me to assent to the conclusion that in one form of cirrhosis there is an interstitial or a lobular hepatitis, in another a perilobular hepatitis, in another that the important pathological phenomenon is inflammation confined to the coats of the duct, and extending from them into the interlobular fissures.

The immense number of degenerating tubes seen in some cases of the disease has led to the supposition that new tubes containing cells are actually formed, and grow and increase in the so-called cicatricial tissue, but it is evident from their drawings and description that the observers who advocate this view have little idea of the number of ductal tubes which are to be demonstrated in the healthy liver of man and animals. In some of the drawings, for example in those accompanying Charcot's Memoirs and his Lectures, intended to indicate a considerable increase of these ductal tubes in morbid changes resulting from tying the duct, the tubes delineated do not, I think, amount to one-fourth of the number to be seen in some well-prepared specimens of healthy liver.

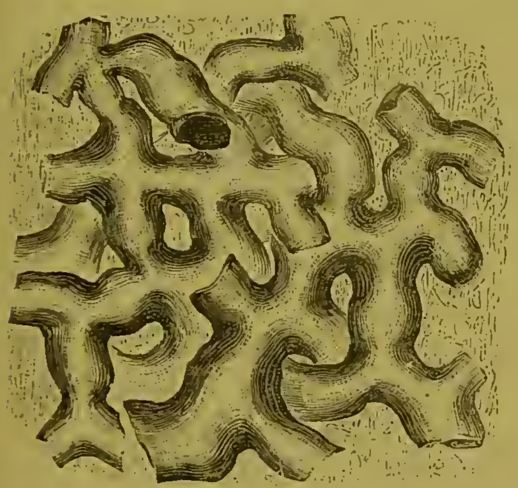
LIVER DUCT OBSTRUCTED.

Fig. 78.



Section of liver in which the common duct had been obstructed for two years before death. Patient aged 40. The ducts between the lobules are much dilated and are injected. The lobules, or the part of them, still contain cells, and are reduced to about half the normal diameter. × 45. p. 187.

Fig. 79.



Capillaries injected. From another part of the same specimen as that represented in Fig. 75, Pl XXII. × 215. p. 76.

Fig. 80.

Central or intra-lobular vein, from a liver in which the common duct was obstructed. The vein and the capillaries of the centre of the lobule are in a normal condition. × 42. p. 187.

Fig. 81.

Small branches of duct in inter-lobular fissure, injected with many of the smallest branches on surface of lobule. From a liver in which the common duct had been occluded for two years. × 15. p. 187.

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Minute Changes resulting from Obstruction of the Duct.—The morbid changes in the liver which sometimes result from prolonged obstruction of the common duct in some respects resemble those occurring in the course of ordinary cirrhosis. Indeed, I have seen sections of such a liver which could not be distinguished from corresponding sections of a cirrhosed liver when carefully examined by the unaided eye or by low (under fifty diameters) magnifying powers. In Fig. 78, Pl. XXIII, a thin section of a liver in which the common duct had been obstructed for two years is represented. The engraving has been copied from a drawing published in 1859 in the first volume of my "Archives of Medicine." When the large ducts of this liver had been carefully injected, many branches were seen in the interlobular fissures, as is well shown in Figs. 78, 81, Pl. XXIII. Upon examination with high magnifying powers, the fine ducts and the cell-containing network were much more easily demonstrated than in the case of the healthy liver. The tubes contained granular matter and oil-globules, but the degenerative changes were somewhat different from those seen in ordinary cirrhosis. See Figs. 84 and 85, Pl. XXIV. The outlines of many of the tubes of the cell-containing network at the margin were even, and though the cells had degenerated and the tubes were narrower, their course and arrangement were exceptionally distinct.

In this liver the vessels were pervious, and but little changed. The duct, artery, portal vein, and hepatic vein were all well injected in different portions of liver. Fig. 80, Pl. XXIII.

Till towards the close of the case blood probably passed through the vessels in every part of the organ, and many of the cells continued to form bile; but, in cirrhosis, degeneration of the cells from the pressure exerted by the accumulated bile gradually proceeds in a direction from the circumference towards the centre of the lobule. The impediment to the circulation during the greater part of the illness was not enough to cause ascites, which only appeared towards the last, and was probably more dependent upon the gradual alteration produced in the blood by the derangement of the liver than to the direct effect of the impeded hepatic circulation. The structural changes in this liver were exceptional, and had probably occurred very gradually.

The supposed Formation of New Ducts in the Cicatricial Tissue.—Whether the facts justify the conclusion of many recent investigators that cirrhosis which arises from inflammation of the coats of the duct is essentially different from ordinary cirrhosis is doubtful. At any rate as regards the smaller ducts and the changes in the cell-containing network continuous with them, I do not think a distinction can be drawn in a sufficient number of cases to justify the general inference in question.

Of course it is possible that some of the large tortuous ducts

figured by some observers may have grown since the cirrhotic change commenced, as seems to have been suggested by Waldeyer in 1868, and confirmed and further extended by Charcot and Cornil, and more recently (1875) by Hanot, in cases of cirrhosis originating in inflammation of the bile duct. But from the description given, and the drawings accompanying the memoirs, it is doubtful whether the advocates of this view were aware of the very considerable number of fine ducts in health. In short, in cases in which the new formation of ducts has been inferred from the number present, it is certain that in health many more exist within the same space.

It is more probable that in some cases of liver disease the liver epithelium extends into some of these ducts, while in other cases the ordinary ductal epithelium increases, so as to render the tubes very distinct, than that they are altogether new ducts formed in the connective tissue developed in the course of cirrhotic changes. The state of things in the lobule undergoing cirrhosis is not favourable, one would think, to exaggerated duct growth, while the growth of ductal epithelium probably would be favoured by the absence of secretion from the ducts.

The suggestion of the formation of new ducts or secreting tubes in the so-called inflammatory lymph or cicatricial tissue would not, I think, have occurred to any one who had a correct idea of the immense number of fine ducts between, and on the surface of, the lobule of the healthy liver. I think as time passes the view that these supposed new duct formations are but the tubes and networks of the healthy structure distended in consequence of impediment to the onward flow of the bile, and otherwise altered, will prove correct. It seems to have been accepted as a true proposition that, because fine ducts were not to be demonstrated when empty, none could exist. Looking from the side of observation only, it is certainly very remarkable that so far-fetched an hypothesis should be brought forward to account for an appearance which would require no such exceptional explanation if only the arrangement in health had been understood.

I hope the observations recorded in this work upon the structure of the human liver in health will be fairly considered by careful investigators of the present day, and that the whole subject of the anatomy of the organ will be reconsidered. Until this has been done there will, in my opinion, be no chance of drawing correct inferences concerning many of the pathological changes in this most important gland. I am convinced that, if any dispassionate observer will only patiently study the many memoirs written during the past few years on cirrhosis and hypertrophic cirrhosis, he will be convinced that no efforts should be spared to clear up questions bearing on the fundamental anatomy and on the action of the liver.

The doubts and opposite views still entertained concerning fundamental questions of arrangement of the ducts and other anatomical elements of the liver deter me for the present from attempting to discuss in detail the nature of many important pathological changes, and incline me to postpone the publication of conclusions concerning the nature and order of the changes in some other forms of liver disease.

Of the Cell Changes in Cirrhosis.—In Cirrhosis the cell changes invariably commence in that part of the cell-containing network which lies at the circumference of the lobule, the tubes of which are directly continuous with the finest ducts. It is these marginal cells which initiate all the important changes in the disease. In consequence, as it seems to me, of more work than usual being thrown upon them, the cells increase in size. After remaining enlarged for some time, their working powers fail, and they begin to shrink. Gradually the cells get much smaller than natural, and soon become quite incapable of performing function. From the circumference of the lobule these cell changes gradually extend inwards towards the centre.

The circumferential part of the network may be wasted to such a degree that the cell remains can only be discovered by special investigation, and in many cases all that remains of the part of the cell-containing network, which was most actively concerned in bile secretion, is represented by small stellate bodies with long branching processes, like some forms of connective tissue corpuscles. As the cirrhotic change advances the altered cell-containing network increases in extent, and the course of the narrow tubes containing here and there only a few cells can be very clearly traced, as shown in Figs. 74, 76, 77, Pl. XXII, towards the centre of the lobule. At the same time that shrinkage of the lobule proceeds, the tubes of the contracted network approach nearer to one another, and as no secretion passes along them many of the tubes become obliterated, and what was once a part of a tube containing several cells gradually becomes narrower and narrower, until the cells and all appearance of a tube are obliterated, and nothing but a mere line remains, which helps with others to produce what has been described as a fibrillated appearance. When two or three cells remain in a portion of the network, and these gradually shrink, an appearance as of a cell with many nuclei and caudate extensions therefrom is produced, and as the contraction further proceeds, the body like a connective tissue corpuscle results. I have traced the several stages of wasting and degeneration from the ordinary cell-containing network to the formation of "connective tissue corpuscles," not only in the human subject but in some of the lower animals. In the frog, as I shall show, the changes corresponding to those I have described in man can be very clearly demonstrated. The evidence appears to me conclusive that in cirrhosis the change

begins in the cells, and the disease ought to be regarded as due essentially to a cell change. The liver-cell is the starting-point of pathological change. The broad alterations, shrinking, hardening, contraction of the hepatic tissue are but the necessary consequences of this cell derangement and degeneration.

In those lobules in which the cell changes have been proceeding rapidly, the ordinary lobular cell network of the liver will be reduced to a small rounded mass in the central part of the cirrhosed lobule often less than one-third of the diameter of the lobule in health, and in extreme cases a mere spot. In many lobules the cells that remain are often found to be larger, and in some instances very much larger, than healthy and active liver-cells. These cells have continued to grow probably for a long time after they had ceased to discharge their bile-forming office. The collection of cells that is left seems to have been for long entirely cut off from any connection with the ductal network and ducts. It is very possible, however, that some cells may still take part in the formation of glycogen, but in most cases they certainly contain no biliary particles or oil-globules, though I have observed in some instances a few of the latter with some small oil-globules.

As I have just remarked, for some time after the degenerative process has been going on, many of the finer tubes connecting the cell-containing network with the duct have been undergoing obliteration, and not a few will have altogether disappeared. Here and there, perhaps, one or two will have remained pervious, and any bile formed would find its way by these into the duct. But in some cases where the pathological changes have been proceeding very slowly indeed, in consequence of the patient being placed under conditions very favourable for living under the adverse circumstances of hepatic disease, even the small residue of cells remaining may disappear, and all bile formation cease. By this time the body will have reached, it may be, an extreme degree of emaciation. The organism, however, having become gradually habituated to a very small amount of food, will be able to subsist even for some time, although much of the physiological work, and especially that performed by the liver, will have altogether ceased. This is an example of a well-known principle that a degree of failure of a vital organ certain to be fatal if suddenly occurring is not inconsistent with subsistence even for a considerable time if only the change shall have been brought about by very slow degrees—a matter worthy of the careful attention of the physician in connection with the treatment of many forms of chronic disease, and of immense consequence in determining how to prolong life to the last moment.

The liver-cells having undergone the degeneration experienced in cirrhosis can never regain their normal condition. The lobular cell-containing network having assumed the characters represented in

Figs. 76, 77 can never be restored to its normal state, or again acquire working power. The degenerated cells may further degenerate, and the residual products be entirely removed, but, as far as is known, under no circumstances whatever can new secreting structure take the place of that which has been removed. Up to a certain period of life no doubt new lobules may be developed, and take the place of lobules that have degenerated, but whether the degenerated tubes and vessels of a particular lobule can be replaced by new cell-containing network, new vessels, or new ducts, after the liver is fully developed is questionable.

Although there is a degree of truth in the statement that in certain pathological formations a return to the embryonic condition is indicated, and undoubtedly in some the cells resemble in general appearance and in rapidity of growth and multiplication those found in some embryonic cell collections, which represent organs undergoing development, it must be borne in mind that they differ enormously as regards power. While in the normal embryonic cell or elementary part there is the capacity for organ—for structure—production, in the new pathological elementary part there is no capacity for evolving anything of use or of advantage to the organism. Growth, tissue-formation, of a kind there may be, but the effect is invariably detrimental. The result most to be desired is the death and quick removal of the adventitious material, for its growth and increase would probably mean chronic derangement or the early death of the organism.

The Causes of the Wasting and Degeneration of the Cells.—The structural alterations which have been referred to, and which are illustrated in Figs. 74, 76, 77, Pl. XXII, are, at least in great part, the consequence not of inflammatory change, but of previous over-action, or a struggle to do more than the ordinary amount of work on the part of the cells. Long before the wasting process commenced, the cells had much increased in size, in consequence of having to take up from the portal blood a larger amount of matter than could be converted into biliary and other constituents in the time intervening between one large meal and the next. The cells subjected to this increased action, especially when continuous or frequently repeated, gradually lose their activity and become deranged, not only as regards their work, but also in respect of growth. Their watery constituents are no doubt soon absorbed. The cell afterwards begins to shrink and gradually becomes much smaller, so that the same space would be occupied by twice or three times as many cells as it would contain in the healthy state. The capacity for cell action after a time is lost, and the degeneration proceeds until all that remains as representing the cell is a small hardened body, with a small scarcely changing bioplast (nucleus), but which can be very clearly discerned in specimens

stained with carmine. At length the last vestige of what was once a collection of thousands of highly active agents concerned in the formation of some of the most remarkable and complex substances known to chemistry disappears, and a cicatrix, an arrangement of irregularly converging lines, is all that is left to mark the seat of the lobule—a highly elaborate apparatus, with a marvellous power of resolving and producing chemical substances having special characteristics, different from any other products formed by living forms, animal or vegetable.

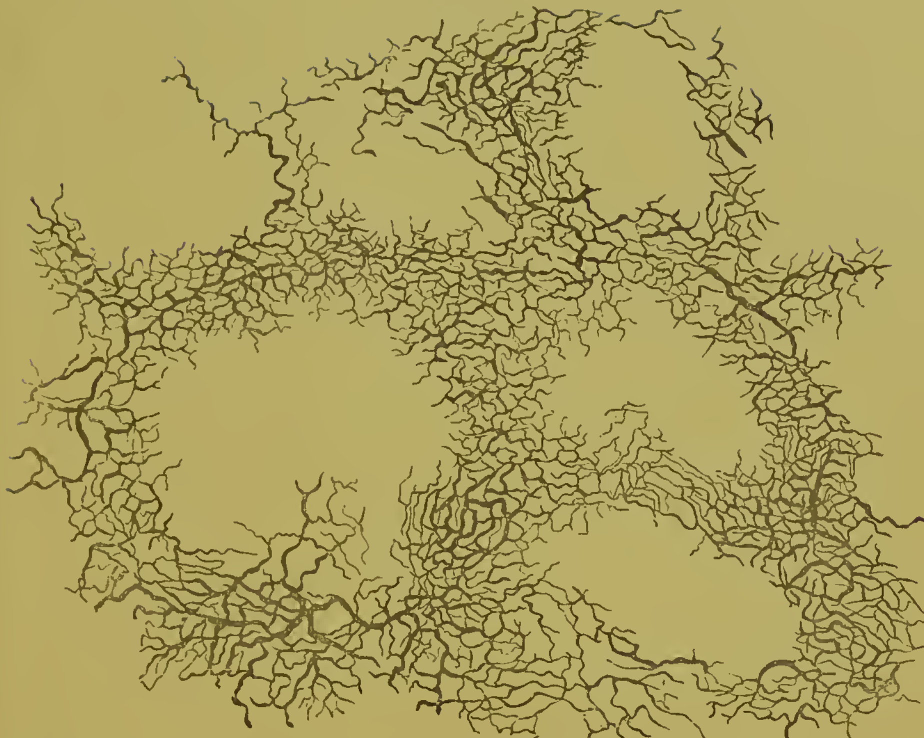
Of the Changes in the Vessels and Capillaries of the Lobule.—Many of the subdivisions of the interlobular branches of the portal vein are enlarged, though many of the capillaries connected with these and resulting from their subdivision waste and are ultimately obliterated. At the same time, in an injection one is struck with the great vascularity of the so-called connective tissue. The appearances presented by a well-injected specimen are seen in Fig. 82, Pl. XXIV. And yet very few indeed of these numerous vascular branches could have been made out in an uninjected specimen, especially if it had been mounted in Canada balsam. If the ducts are also injected, numerous branches will be demonstrated. The greater number probably subserve no purpose now that the secreting structure connected with them has degenerated. But the fact of the presence of these ducts is important, for it shows that at least a considerable area of what has been regarded as mere fibrous cicatricial tissue, the result of inflammation, is freely penetrated in all directions with branches of vessels and ducts, and therefore that it is not wholly adventitious, resulting from inflammatory action, but contains some of the elements of the normal hepatic structure.

Many of the capillaries in the outer part of the lobules, after having been unduly distended for a time, have, like tubes of the network, undergone change, the blood being diverted to lobules which still continue actually healthy or are nearly so. The capillaries shrink, their walls undergoing fatty degeneration, and many of the tubes becoming impervious. Fig. 83, Pl. XXIV. In some the walls represented are seen to be thickened by the addition of hard fibroid material, which is incorporated with the fibrous matter of which the cell-containing network is mainly composed.

Thickening and Adherence of Capsule—Fissures and Eminences.—The thick and firm condition of the capsule of the liver in cirrhosis is well known. Like other morbid changes in the liver this has also been attributed to inflammation. The thickening of the capsule seems to be due mainly to the wasting and degeneration of many of the superficial lobules. The remains of the old tubes of the cell-containing network can often be detected in the fibrous structure of the deeper part of the capsule. As wasting goes on, the *débris* of many lobules

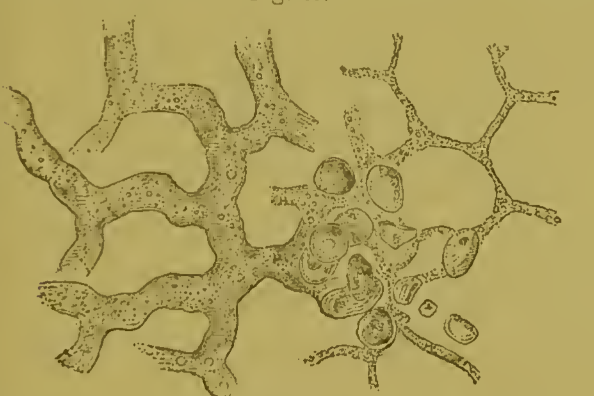
CIRRHOSIS.

Fig. 82.



Portal vessels of a cirrhosed liver injected. The lobules are not represented in the drawing. The spaces do not correspond to separate lobules, but in the large ones several lobules have been as it were fused together. Each space is completely surrounded by vessels, but very few branches enter the lobules. × 15. p. 192.

Fig. 83.



Degenerated and wasted capillaries from the lobule of a cirrhosed liver. To the left the walls of the capillaries contain numerous granules and oil globules, while on the right the capillaries have almost disappeared. × 215. p. 187.

Fig. 84.

Ducts and commencing portion of the cell containing network of lobule from a liver in which the common duct had been obstructed for two years. The liver cells have wasted, leaving the tubes very narrow. They contain only granular matter and oil globules. × 150. p. 187.

Fig. 85.

A part of the cell containing network from the same liver as Fig. 84, showing complete absence of cells, the tubes being very narrow and containing granular matter and oil globules only. × 130. p. 187.

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remains, and helps to increase the thickness of the capsule. In the small liver of young animals, and at an early period of development in all, it can scarcely be said that a capsule exists. So thin and delicate is the membrane on the surface of the liver that it appears to consist of peritoneum only. As development proceeds and the liver enlarges, the superficial and earliest formed lobules degenerate, and their *débris* serves to increase the thickness, opacity, and fibrous character of the so-called capsule.

In many cases of cirrhosis change in the lobules proceeds apace, and the capsule gets thicker and thicker as the disease advances. As the lobules are intimately connected with one another (p. 67), their fibroid remains will, of course, be connected. No wonder then that when we attempt to strip off the capsule it is found to adhere very firmly (as is said) to the hepatic tissue, or that the latter is torn asunder, and portions adhere to it when attempts are made to strip off the capsule.

In health portions of the structure of the subjacent lobules are detached with the capsule, but in cirrhosis, as degeneration has affected many layers of lobules, the firm fibrous *débris* does not yield like the soft structure of the healthy lobule, and many layers of degenerated and partly degenerated lobules adhere, and can only be torn from one another if considerable force be employed. In all parts, however, there is loss and condensation of tissue. Irregular hardening, thickening, and puckering occur, and thus fissures of considerable depth are often formed on the surface of the liver. As I have before remarked, it seems to me more probable that the depressions seen between portions of hepatic tissue are due simply to the gradual wasting and removal of substance which was once in an active and healthy condition than to the contraction and shrinking of tissue following inflammatory change. This causes irregular contraction. The large irregular eminences, often seen on the surface of the liver in certain cases of cirrhosis, known as "hobnail liver," are due to the irregular wasting referred to rather than to contraction of fibroid tissue. Although in some cases the change is in as well as around the lobules, and in others mainly around or between them, I do not think there is sufficient reason to divide cirrhosis into an intralobular and a perilobular form of the disease.

The firmness with which the capsule adheres to the hepatic tissue is very remarkable, and this fact is always observed in cirrhosis. The adherence is usually attributed to inflammatory changes affecting the fibrous capsule, and extending from this inwards into the hepatic tissue. But what is the capsule, and how is it formed? Like the "connective tissue" around nerves and muscles, it is formed by the gradual accumulation of *débris* of tissue, which was active at an antecedent period.

The faster the organ lives the thicker will be the fibrous capsule. In cirrhosis the wasting and degeneration of adjacent lobules contribute to the increased thickness of the capsule in this disease. If the deep aspect of the capsule be carefully examined, not only may the remains of ancient lobules be detected in its substance, but the partially wasted cell-containing network of lobules only recently degenerated may be demonstrated in properly prepared specimens.

If, however, thin sections of this tissue, which have been properly treated in carmine fluid, be soaked for a considerable time in glycerine, by which medium they will be rendered transparent, and examined under a quarter-of-an-inch object-glass, the structural arrangement of a remarkable and very well-defined character, which I have described and which was before quite invisible, will be very distinctly observable.

Cirrhosis in the Lower Animals.—The views I have advanced concerning the nature of the changes taking place in cirrhotic contraction or wasting of the liver receive interesting confirmation from the study of the alterations I have demonstrated and figured in a very contracted frog's liver. The animal had been many months in confinement, and died in a state of emaciation. The liver was less than half the normal size. Its texture was unusually firm, and to the unaided eye it had a very pale and fibrous appearance. I injected the duct and obtained some excellent preparations, showing considerable thickening of the walls of these tubes. In some places the injection had passed on to the cell-containing network. One of the specimens, figured in Pl. XVII, Fig. 51, p. 114, will illustrate the appearances observed. The continuity between the true ducts and the tubes of the cell-containing network is very distinct in this preparation, but I think many of the tubes figured in the specimen, which contain ductal epithelium and would now be regarded as truly ductal, at an anterior period contained secreting epithelium where ductal epithelium now is. The part of the tubes in the specimen containing ductal epithelium is more extensive than it is in the healthy frog's liver. It is very probable that under certain circumstances the cells of ductal epithelium may increase in tubes previously entirely occupied with secreting epithelium, while under other conditions the latter may increase in a direction towards the ducts, the ductal epithelium disappearing. The tubes which were once ductal would then constitute the circumferential part of the cell-containing network.

In the livers of old horses the hepatic tissue undergoes great shrinking, and not uncommonly a thin layer of fibrous-like tissue extends for two inches or more beyond what appears to be the edge of the liver. This fibrous-like tissue is in fact all that remains of the outer marginal portion of the liver, and it contains the degenerate remains of true hepatic structures. The ducts which ramify in it may be readily injected

and their numerous anastomoses demonstrated. Many of the networks filled with injection, and for the most part destitute of epithelium, were once part of the cell-containing network of lobules. This is no doubt the explanation of the injection of the ducts obtained by Kiernan, and upon which his view of the arrangement of the ducts, which I hold to be in the main correct, was based. I have copied Kiernan's figure of ducts in the lateral ligament of the human liver in Plate XI, Fig. 36.

In old dogs I have demonstrated a corresponding series of facts, and in most animals, certainly in most domestic animals, in old age a similar disposition of ducts and altered remains of the cell-containing network of the lobule is often demonstrable.

Dr. Greenfield describes the results of examination of two cases of cirrhosis in cats in the "Journ. Comp. Path.," December, 1888. These he considered to be examples of "hypertrophic" or "biliary" cirrhosis, though there was no jaundice. The plexuses of biliary ducts which were injected he regards as new formations—an opinion which, however, I do not think necessarily follows, at least as a general proposition, from the observations recorded. It is possible that the ordinary minute ducts in such cases may be extended,—increased in length, and that diverticula may here and there grow from them. Certain forms of cancer no doubt consist essentially in this extravagant ductal growth, but the condition of things in cirrhotic change is not favourable to such alterations, while the observed facts appear to me to be satisfactorily explained without calling in the aid of what I cannot but regard under the circumstances as a rather far-fetched hypothesis, in this case certainly needless even for working purposes.

Degeneration and wasting of the lobules of the liver resembling the cirrhosis of man and mammalia also occur in birds, and most animals which have been long kept in confinement suffer from similar pathological changes, especially where sufficient care has not been exercised to prevent over-feeding, and more stimulating rich food has been given than is good for the animal. In fowls certainly cirrhotic disease is common.

Summary of the Minute Changes in Cirrhosis.—To sum up the essential changes which take place in the lobules in their progress to the degenerated and wasted condition of advanced cirrhosis:—In the healthy lobule the network of tubes containing the secreting cells alternates with and is exactly fitted into the meshes of the vascular network. The walls of the capillaries at certain points are in close contact with the walls of the tubes of the cell-containing network. But while the two membranous walls in some places touch one another, and are probably incorporated to form one layer, there is no doubt that here and there spaces exist, and that fluid may pass through the vascular walls and distend them. I have forced injection into these spaces from the

lymphatics, and probably enlarged them by the process. It is probable that there is direct communication between these intertubular spaces and the lymphatics.

In cirrhosis the walls of the capillaries and of the tubes of the cell-containing network are often much thickened, and are firmer and less yielding than in the healthy state, so that very thin sections of perfectly fresh tissue can be obtained with a sharp knife, in which the relation of the structures to one another is not much altered, as is invariably the case when an attempt is made to cut thin sections of healthy liver without previous hardening. In advanced cirrhosis, between some of the capillaries and the tubes of the network there exists a little fibrous-like tissue, consisting partly of the altered walls of the tubes and capillaries, partly of newly formed adventitious material. Sometimes this compound tissue attains a thickness of 1-5000th or 1-6000th of an inch. It is to be observed too that not only are the tubes of the cell-containing network narrower and firmer in the cirrhose than in the healthy condition, but, owing to the narrowing of the tubes, the meshes of the network are much wider, and the disposition of the tubes is more irregular. In some places the tubes are as wide as or wider than in health, in others so narrow are they that they seem to be mere threads. It must, however, be remarked that in the healthy liver the tubes of the cell-containing network in some situations are much below the average width. This is constantly observed in the fœtal liver at a time when the network is being developed, and before the cells have reached their normal size. It would seem, then, that in the embryo liver the tubes and cells are at first narrow, and as development proceeds increase in diameter. In the wasting which occurs in cirrhosis the large cells and wide secreting tubes shrink, and are gradually much reduced in diameter. This wasting and contraction may be studied in its different stages in many cases of cirrhosis, and in an extreme case a stellate or spindle-shaped corpuscle with the fibrous-like tissue adjacent to it is all that remains of a portion of hepatic tissue, consisting of capillary vessels, cell-containing network, and its secreting cells.

It seems to me that these observations on the cirrhose liver confirm the view that the tube of a secreting gland with its secreting cells may degenerate into what is generally known as a connective tissue corpuscle. Whether we study the appearances observed in the human liver or in that of many of the lower animals, the conclusions I have drawn will receive support. Moreover, corresponding morbid changes have been studied in many other glandular organs, and the same general conclusion presents itself to the mind.

In the long course of events, the first change is enlargement of the liver-cells, the bioplasm in particular undergoing increase. The relative proportion of formed material to the bioplasm is less than in healthy

cells. The cell ceases to discharge its function and then shrinks. Shrinking, hardening, and degenerative changes gradually ensue in all the hepatic tissues, and, if the patient lives, the whole liver slowly wastes, until at last what was once a highly active rapidly changing organ becomes a small mass of very hard, passive, fibrous-like tissue, no longer able to perform any function whatever, incapable of regeneration or improvement, and perfectly useless to the organism, the death of which must soon result from the morbid changes which have run their course in this important gland.

OF THE CONSEQUENCES OF HEPATIC INFLAMMATION AND DEGENERATION, AND OF THE PRINCIPLES OF TREATING THE SICK.

Changes which commence in congestion, and which may result in local inflammation or abscess, or in general rapid enlargement of the liver, with exudation, damage to the liver-cells, and complete destruction of normal gland tissue, must needs engage the serious attention of physicians, especially as it is only in the commencement of the pathological action that complete restoration to the normal condition can in general be expected. The persistence or increase of the morbid action may result either in early death from the intensity of the liver disturbance, or in chronic disease, which must destroy health and working power, and cut short life. The arrest of initial phenomena which lead on to pathological changes of such intensity and gravity is therefore all important. The principles upon which the treatment of the early congestion should be based have been already considered in page 140.

The diagnosis and treatment of acute and chronic abscess of the liver rest upon well-ascertained principles, but difficulties often present themselves in practice, and sometimes many attempts are made before the pus can be reached. As this part of the subject is fully discussed in many standard medical works, I do not propose to consider it here.

The most frequent cause of ordinary cirrhotic change, as has been already explained, is over eating and drinking, and very irregular living extending perhaps over many years. Even in the case of those who are moderate, the habit of eating one large meal daily is, I believe, a very frequent cause of disease in persons who consider themselves careful as regards living, and who certainly have never exceeded in the matter of drink at any period of life. Man's liver, as has been shown, is not constructed on the principles which obtain in the liver of the pig (p. 67), an animal which may gorge with impunity, and is capable of very quickly assimilating enormous quantities of highly nutritious food. Man is not a gorging animal, and some among us get on best when small quantities of food are introduced four or five times in the course

of twenty-four hours. The human liver, though large, and, as I have said, capable of accommodating itself to a very varying amount of work without suffering in structure, is liable to derangement and actual damage if a very unusual quantity of portal blood is carried to it within a short period of time.

The introduction of more food and stimulants than the body requires does not usually set up inflammation, as is often stated, but causes slowing of the blood-flow through the capillaries, and the accumulation of vast quantities of blood in the extensive capillary networks of the lobules, pressure upon the cells, which at first enlarge in consequence of taking up matter faster than it can be converted into products of secretion, and then fail altogether in action, and shrink and degenerate. After some time depurated blood gets into the systemic circulation, and all the nutritious and formative processes are more or less deranged.

Looking, therefore, merely from the pathological and purely scientific standpoint, all should be encouraged in their efforts to spread physiological knowledge concerning the quantity and kind of food required for health, and especially to force on the attention the fact of the wide-spread evil habit of over eating and drinking still terribly prevalent in the masses as well as in the classes of the people, particularly under conditions of life as obtain in the case of hot climates, rendering all excess doubly hurtful.

Serious portal and hepatic congestion may be very soon relieved by free purgation, and impending hæmorrhage may be prevented even in serious cases if the bowels can at once be made to act freely, but in already damaged organisms the greatest care must be taken not to exhaust the patient's strength. Even in the very weak, a strong drastic purgative may be given with advantage, if, at the same time, alcohol be allowed. And especially is it important to bear in mind that many of the persons suffering from this form of disease have long been free livers, and their system has got into the habit of using up far more nutrient matter than is really required for a healthy man. Not a few have been inveterate alcohol takers, or even drunkards. Alcohol, at any rate for a few days, must be given, and sometimes in large quantity, as well as purgatives, if the life is to be saved. And it is well to bear in mind that a certain quantity of alcohol, with products resulting from its change in the blood, does not cause nearly the same amount of harm to the patient that may result from the continued accumulation in the blood of those highly deleterious substances that may be quickly removed from the circulating fluid by a brisk purgative. This highly important question in its many bearings must be carefully considered by the thoughtful practitioner in each individual case, and the precise action must be determined after a comprehensive survey of the several facts.

He must, however, be careful not to underestimate the enormous importance of the principle that decided and quick elimination is of all things needful, and especially in cases in which the hepatic disturbance has advanced rapidly and is severe.

As is well known, cirrhosis may cause death in the early stages in many ways. If serious symptoms have come on very quickly, the patient may die of blood-poisoning. Convulsions and coma may supervene. Violent hæmorrhage from the capillaries of the stomach and part of the small intestine may cause fatal syncope. It is, therefore, of great importance to note the state of the pulse and the force of the heart's action from day to day, and to keep the patient quite still in the recumbent posture as long as there is any fear of hæmorrhage.

In some cases, it may be necessary to give ammonia and alcoholic stimulants in order to keep up the force of the heart, and thus prevent the blood from stagnating in some of the capillaries.

With regard to the secondary results, and almost necessary consequences, of the chronic cirrhotic state, there is very much to be considered. For it is certain not only that the duration of the patient's life, but his comfort during the time he has to live, will greatly depend upon his medical management. Some forms of cirrhosis are undoubtedly incurable even from a very early period, but we must remember that not a few incurable cases have to live for many years, and that it is in our power greatly to help patients under the above conditions. Not only so, but disease both of liver and kidney which is not to be cured is not inconsistent even with enjoyment of life, if only the patient will be reasonable and submit to be guided by rational consideration. Of course, if a patient with cirrhosis cannot be persuaded to forego the pleasures of the table, and will persist in eating and drinking too freely, if he will have his four or more pints of beer daily, it is beyond our power to be of much real help to him. I have heard that life is not worth having if free living is to be denied, the regimen objected to being far more liberal than many of the hardest working and most distinguished men have taken or desired all through a very long and useful life, but I am incompetent to form a judgment upon this question.

A disease which results in impaired function of an important organ and irreparable structural change must inevitably cause serious derangement of other tissues and organs of the body, and, indeed, disturb all the ordinary physiological processes. The composition of the blood will soon be affected. The nutritive processes will be deranged, and the action of all the active tissues of the body more or less disturbed. The structural change, the wasting and degeneration of hepatic tissue, cannot be repaired or compensated, but the length of the patient's life may be increased by good management, and his activity and comfort may be greatly promoted.

Ascites.—Among the common and sometimes early consequences of cirrhosis is ascites. The usual explanation of the transudation of serous fluid from the blood into the peritoneal cavity is no doubt in the main correct, but it is very desirable that we should learn why in one case the vascular tension appears to be relieved by extensive hæmorrhage from the capillaries of a large tract of mucous membrane, and in another by the gradual pouring out of serum only, and often very weak serum, from the vessels of the serous membrane; why the tension is not more often relieved than is the case by serous effusion only from the capillaries of the mucous membrane; why the catastrophe of hæmorrhage into the peritoneal cavity is happily so very uncommon. The slow degenerative changes in the arterial, venous, and capillary walls which have been steadily progressing for a long while previously will, no doubt, account for sudden capillary hæmorrhage, but the facts cannot be wholly explained by this supposition.

In general, the serous fluid which transudes through the capillaries from the blood contains a larger percentage of salts and a lower percentage of albumen than is found in the ascitic fluid which has been accumulating, and which has perhaps remained some time in the peritoneal cavity. But the concentration which occurs in the case of ascitic or pleuritic fluid is greatly surpassed by the very viscid serous fluid in ovarian and other cysts. In this case, it is possible that the corpuscular elements in the fluid act like secreting cells. Although the fluid poured into a serous cavity accumulates too quickly to be separated from the blood by a process akin to secretion, it is not unlikely that in chronic cases corpuscular elements on the inner surface of the serous membrane are concerned in the process, and it seems not improbable that these, having grown and multiplied, are the active agents in drawing nutrient matters from the blood, and forming some of the constituents of those forms of ascitic fluid found after the condition has existed for some time. The corpuscular elements in question are in the main probably derived from the bioplasm of the blood (colourless blood corpuscles), and from the minute particles of the same character invariably present in immense number in the circulating fluid; but some, perhaps, may have sprung from the bioplasm of the structures of the serous membrane itself. The bioplasm from both sources would, we know, be competent to form albuminous matters, as well as substances which at length become converted into a gelatin-yielding fibrous matter.

The stretching to which the abdominal walls are subject in many cases of ascites consequent upon cirrhosis is very remarkable, and cannot be imitated artificially, while so far it has not been adequately explained. It is difficult to see how this tension could result from mere transudation of fluid from the blood-vessels, but if any process akin to secretion, like that above suggested, were concerned, the fact would be

easily accounted for, and in favour of this view it must be borne in mind that from leucocytes or smaller particles of bioplasm which pass through capillary walls, bioplasts of considerable size and number undoubtedly result in a great many conditions, while certain serous cysts which contain highly concentrated albuminous fluid seem to originate in small extra-capillary spaces, and it seems, upon the whole, more probable that the elements concerned in changes within the cavity originate from the bioplasm of the blood than from any epithelium which belongs to lymph spaces, vessels, or glands.

That fluid may be poured out from the blood into a serous or other cavity in consequence of an obstruction to the return of blood in the veins is certain, and pressure on a vein, or a plug of fibrin even partially occluding the vessel, will cause an increase of fluid in tissues as in ordinary œdema. But weak serum may escape through the capillary walls, and in large quantity, in consequence of changes in the blood only, irrespective of pressure or any alterations in vessels. The blood changes in question are usually effected very slowly, and extend over a considerable period of time, but when they have reached a certain degree, the escape of fluid in considerable quantity may occur at almost any moment, and the precise seat of its escape seems to be determined by almost accidental circumstances, such as slight local injury, some slight developmental imperfection in a part, or some slight pathological change in tissue. Depression of the heart's action from fatigue, and the sudden introduction of cold damp air into the lungs, may cause the pouring out of much of the accumulated morbid fluid into the lung. Or under slightly different circumstances a pint or more of fluid may very quickly collect in one or other pleural cavity, or overworked muscles and adjacent tissues may be the seat of effusion. Or the fluid holding in solution various materials may be poured out into the alimentary canal, in which case a diarrhœa, or pouring out of fluid into the stomach followed by vomiting, restores the patient to health. Such considerations not unfrequently suggest principles upon which the treatment of cases may be successfully conducted. In cases where effusion of fluid in tissues or in a serous cavity is impending, by the timely administration of a simple quick-acting purgative, we may succeed in effecting a beneficial change which will at once be followed by a quick return to the healthy condition, it may be after the patient has been ailing for a considerable time.

The local or general escape of weak serum from the blood may also occur irrespective of obstruction in any part of the venous system, and without any departure from the healthy state of the blood itself. Nerve changes alone will bring about an alteration in the arterioles, and, as a consequence, in the capillaries, rendering the escape of serum through the walls a certainty.

Relaxation of the muscular fibres of the arterioles is followed by dilatation of the capillaries. The increase in diameter of the latter is necessarily associated with corresponding stretching and thinning of the capillary walls, and the congestion may be carried to such a degree that not only serum but blood may pass through.

It seems to me certain that in many local congestions, inflammations, and œdema, the first step in the change which results in congesgestion, exudation, extravasation, in many cases occurs not in the nerve-centre nor in the trunks or fine fibres which ramify amongst the muscular fibre-cells of the arterioles, but in the peripheral nerve network of the parts affected, the particular nerve-fibres involved being those which I have shown to be contiguous to the capillaries, and which in some tissues are in great number, and from which network efferent fibres proceed to the nerve-centre. Not only therefore may effusion of serum in a tissue result from changes in the tissue itself, but the afferent nerve-fibres running close to the capillaries of certain parts may be disturbed by certain materials in the blood itself which have passed through the capillary wall with the nutrient matter. The disturbance of the afferent nerve-fibres is followed by change in the nerve-centre, and responsive influence transmitted by the efferent nerve-fibres may result in contraction of the muscular fibres of the venules or relaxation of muscular fibres and dilatation of the arterioles, or in both—to be soon followed by the local escape of serum from the blood.

Now, in cases of cirrhosis in which ascites comes on at an early period, is it not more probable that the ascites is occasioned by the reflex action of efferent nerves in the liver disturbed by the pathological changes that have been going on for some time, than that it is due solely to the physical obstruction of the portal vessels? In the rapid enlargement of the liver, which is observed in some acute cases, this would surely be the most reasonable explanation of the pouring out of the fluid in the peritoneal sac. No doubt where the ascites appears late, and the liver is much contracted and hardened, the portal vessels are considerably constricted, but even in these cases the pouring out of fluid is not the simple physical process it is often claimed to be. The blood is greatly changed from the long illness the patient has experienced, and without doubt in many of these cases the fluid part of the blood too readily permeates the capillary walls. It is very remarkable that occasionally we observe the tendency to effusion of serum passing away, and I have noticed more than once that this desirable change has been associated with improvement in the general health consequent upon change to more generous living and good air, and taking some preparation of iron.

Changes in the blood itself, impediment to its free passage through

the portal vessels, and alteration in the capillary walls, all contribute to the production of ascites in many cases. Probably in most instances, however, changes in the capillary walls have been proceeding for a considerable time, and not uncommonly numerous minute oil-globules, solitary and in collections, may be detected in the transparent tissue by careful microscopical examination with powers of 300 diameters and upwards. The sudden and sometimes fatal hæmorrhage which occurs from the capillaries of the mucous membrane is preceded by such alterations, and it is certain that the degenerative changes have more to do with the escape of the blood than undue pressure upon the vascular walls.

In hydræmia, as the condition in which the blood contains an undue proportion of water is called, diluted serum may quickly filter through the capillary walls in considerable quantity, and at least in this condition the watery blood must be regarded as the cause of the dropsy. In certain forms of œdema and in cases of accumulation of fluid in serous cavities, there is good reason to think that change in the blood is the chief factor in the production of dropsical effusion. On the other hand, many cases may be pointed out in which the effusion seems to be due to partial obstruction to the venous circulation only. In many cases of ascites, consequent upon cirrhosis, no doubt impeded circulation through the liver and important changes in the blood both contribute to the result. In discussing this question, we must not fail to take into account the fact that now and then a case of cirrhosis is met with in which there has been very considerable impediment to the blood-flow through the liver, but which is not attended with ascites from first to last, while, on the other hand, ascites sometimes comes on early and proceeds to a considerable degree in cases which are not characterised by more than very moderately impeded portal circulation. The problem is more complex and more difficult of solution than is generally supposed. At the same time there is little doubt that by a very slight alteration in the blood and the condition of the vascular walls the escape of serum into the peritoneal cavity may be prevented, and I am inclined to think that by free purgation and diuresis, excited at an early period, in cases in which the kidneys are healthy, ascites may occasionally be prevented altogether; but unfortunately we are not always able to decide whether this desirable result is actually brought about by the treatment or is due to other circumstances, nor can we determine beforehand the particular cases in which this highly satisfactory effect is likely to be attained.

The reader will find many points connected with dropsy discussed in an interesting memoir on the nature and treatment of dropsy by Dr. James Barr in the "Liverpool Medico-Chirurgical Journal" for July, 1886.

Treatment of Ascites.—Purging, diuresis, and sweating are all useful at an early period of the disease in certain cases, but of course the practitioner must be guided in these, as in other modes of treatment, by patients' general condition and strength, and by other matters. Violent purging may do great harm, and even cause death, while in some cases life may be saved by this proceeding. No doubt, as has been remarked, mischief might result from the indiscriminate use of these and indeed any other method of treatment, but who in these days practises in a manner to deserve such animadversions ? Those who talk thus almost insinuate that many practitioners they have known or heard of treat disease in a thoughtless, haphazard sort of fashion, and are as likely to do harm as good by therapeutic interference.

Sudorifics can only be of service in ascites in an indirect manner. Any medicine or food which is calculated to improve the quality of the blood will favour the absorption of the fluid that has been poured out. By sweating, excited by heat or by medicine, noxious matters that have been accumulating in the blood may be removed, and the circulating fluid, in consequence of their removal, will be in a better state to take up transuded serum.

In treating many forms of dropsical effusion, we must bear in mind the important principle that the pouring out of exudation is favoured by a low state of system, and that the absorption of fluid already effused is promoted by the healthy condition. If, therefore, in many cases in which the patient is exceptionally weak, more especially if he has been living low for some time, we continue to administer purgatives and diuretics, and notice that he gets worse instead of better, we shall find that port wine, good strong soup, and tonics must be ordered, and the reabsorption of the effused fluid will proceed apace. It is even possible that a reduction in the diameter of the capillary blood-stream and an increase in the rate of its movement, may occasion a flow through the capillary wall from the outside, in place of a movement of fluid in the opposite direction ; or, in other words, absorption may take the place of transudation. In the treatment of all cases the physician must study the important points in each individual instance, and decide as to treatment after careful consideration of the general facts, rather than attempt to modify the one pathological process which constitutes the chief characteristic of the disease.

Of the value of diuretics in the treatment of a slight and moderate degree of ascites and some other dropsies there can be no doubt, and in cases in which the kidneys are healthy, great benefit may result from the use of the old and well-known pill consisting of blue pill, powdered squills, and digitalis. It is remarkable how very slight a change will sometimes convert a process of local effusion into one of absorption, or *vice versâ*. A slight alteration in the calibre of the arterioles or,

as has been before remarked, in the changes induced in the afferent nerves of the tissue by which the state of the nerve-centre from which the nerves to the arterioles proceed is determined, will be sufficient to cause or stop a pathological process.

Paracentesis.—In many cases, however, we shall find medicinal and other treatment fail to stop the effusion into the peritoneal cavity, and we shall be obliged to relieve the patient by removing the fluid. The first tapping for ascites should not be postponed until the abdominal walls are much stretched and the skin rendered smooth and shiny from the extreme distension. The operation as performed in these days is entirely devoid of danger, and does not cause pain or discomfort. A small cannula is used, and with it is connected a long india-rubber tube by which the fluid is conducted to a large pan placed under the bed. By this arrangement the fluid is drawn off very slowly and there will be no risk of fainting or other disturbance. The slight wound that is made closes at once, and will be completely healed in a few days. If, as unfortunately happens in some cases, more fluid is poured out soon after that which first collected has been removed, the patient must be prepared for a repetition of the operation. If the precautions above referred to are taken, no harm results from the second tapping being performed a few days after the first. In short, it is better to remove the fluid as it collects, or at any rate some time before the peritoneal cavity is nearly full, and the abdominal walls are stretched.

Although frequently the fluid collects again and again, and paracentesis must be repeated after a longer or shorter interval of time, while sometimes the pouring-out of fluid actually increases in the rate of its discharge after it has been several times removed, it does occasionally happen that after two or three tappings a change for the better occurs. In the course of a year or so one may see two or three instances where no further collection of fluid takes place, and the patient recovers.

The quantity of fluid which will collect in the peritoneal cavity is sometimes very great, amounting to more than a hundred pints, and in some cases the rapidity with which it is secreted is very remarkable. Harley refers to one from which twelve gallons of ascitic fluid were secreted in the course of thirteen days.

Tapping is sometimes curative. Occasionally no fluid is poured out after relief by the first tapping, but the explanation of this unfortunately exceptional circumstance has not yet been found. In most cases the fluid collects again, and may be removed perhaps three or four times, but even in this case an occasional instance of permanent relief occurs. I have known the accumulation of fluid to cease after the patient had been tapped more than seven times during a period of two years or more, but I could not explain why, for at no period of the case were there any exceptional facts or occurrences which led me to look for so

very desirable a relief. This happy change in the progress of the disease is sometimes due to restoration of the impeded circulation by the dilatation of venous branches which establish communications between the portal and systemic systems, but in all probability more commonly to changes in the characters, and to the considerably reduced quantity of the blood in the body generally, consequent upon reduction in the activity of the blood-forming process which occurs in all forms of chronic cirrhotic processes.

The fact then of the occurrence from time to time of successful cases leads to the suggestion, and justifies the hope, that with greater care in the medical management of each case, more particularly as regards the general condition of the patient, the proportion of such cases to the whole number of sufferers will be increased.

It seems possible that by diluting the serum by injecting warm distilled water into the peritoneal cavity while it is yet in small or only moderate quantity, not only might further effusion be prevented, but that the absorption of the diluted serum might follow. Very dilute antiseptic fluids might perhaps have the effect of preventing further pouring out of serous fluid from the blood. The wonderful advance of abdominal surgery during the last few years encourages the belief that ere long new and successful methods of treating ascites will be discovered. This conclusion is supported by the new plan of washing out the peritoneal cavity in some cases of peritonitis, which has been successfully carried out in several instances. It has been thoroughly proved that surgical interference involving injury to the peritoneum is not attended with the serious risk of inflammation universally held to obtain only a few years since. Progress in the direction indicated will no doubt be slow, as the greatest care must be taken in the selection of the cases for appropriate treatment. The prolonged suffering and inconvenience entailed by the rapid accumulation of fluid, and the necessity of frequent tappings, with the certainty of the gradual exhaustion of the patient's strength, unquestionably justify the adoption of new methods of treatment affording a reasonable prospect of relief, to say nothing of promise of cure.

In general, the further progress of many cases of ascites is uncertain and variable. In some the improvement is as quick as it is unexpected, while in other cases the steady progress from bad to worse cannot be arrested. And although by judicious management we may sometimes effect recovery, in many we can only hope to prolong life, while not unfrequently we meet with cases in which all our efforts fail to check the progress of the disease, and our usefulness is limited to reducing suffering and discomfort. Much undoubtedly may be done by the physician, not only to prolong life in cases of cirrhosis but to make life not only tolerable but useful and even pleasant. The unexpected

improvement which is now and then observed in advanced cases of the disease, and the cessation of further secretion of ascitic fluid in cases in which such a result appeared for many months very improbable, should encourage us in making more minute study of all the circumstances which can possibly contribute to so favourable a result, as it is very probable that not a few of the cases which do not look very hopeful at the outset may have a different appearance after careful management for a few weeks or months.

METHODS OF INVESTIGATING THE STRUCTURE OF THE LIVER IN HEALTH AND DISEASE.

As success in demonstrating the minute structure of the liver entirely depends upon the methods of preparation to which the tissue is subjected, it is important to consider the principal means by which we render evident the several elements of hepatic structure in health and disease. So many different processes have been advocated by different observers that I shall direct the reader's attention to those only which have been most useful and which have yielded uniform results. I have myself tried many plans which rest on very different principles and which have not been referred to in this work. I propose to describe the special methods adopted in my own investigations in detail sufficient to enable one with ordinary skill and patience who may be interested in the enquiry to practise them with success. It is by the aid of these that the specimens were prepared from which the drawings illustrating my memoir have been taken.

Of Preparing Specimens to show the Continuity of the Ducts with the Tubes of the Cell-containing Network of the Liver.—Although I have succeeded in a few instances in demonstrating the arrangement of the ducts and the cell-containing network in a liver without special preparation, it is so very seldom that demonstrative specimens are to be obtained in this way that special methods must be resorted to. Only now and then, and as it were by accident, can one obtain a thin section from a perfectly fresh liver which shows any of the finest ducts at all, and which the observer could regard as clear and conclusive. If we consider the soft state of the fresh liver and the great difficulty of cutting sections sufficiently thin to be transparent, we shall not feel surprised that special processes have to be resorted to, or that very different views concerning the fundamental structure of the liver should have been accepted and taught.

Unfortunately the matter is further complicated by the circumstance that some authorities decline to admit anything as an anatomical fact which has not been demonstrated in fresh specimens, and altogether object to observations made upon textures which have undergone previous preparation, forgetting that the water in which they prefer to immerse their specimens often exerts a more powerful influence, by completely destroying or altering the natural condition of the structure, than many of the fluids to the use of which they are opposed. The alteration in the appearance of a structure effected by the refractive power of the medium in which it is immersed is often very great, and

must be taken into consideration in examining such preparations as very thin sections of liver.

The same thing, as is well known, presents a very different appearance, according as it is examined in air, water, glycerine or syrup, although neither of these media may have any chemical action on the substance immersed. Again, a delicate tubular membrane will entirely collapse in a limpid fluid like water, while in syrup or glycerine it would retain its original appearance, only it is requisite that, if examined in the latter fluids, plenty of time should be allowed for thorough soaking, and the specimen should be immersed in weak solutions first and the strength gradually increased as the fluid permeates the tissue. In water the tubular character of delicate thin-walled tubes would be lost, while in syrup or glycerine it would remain distinct. It is important to consider such points in practical work.

Hardening the Liver.—In order to show the minute structure with any approach to clearness and certainty in an uninjected specimen, it is necessary to harden the liver, either by freezing or by the chemical or physical action of certain substances. Thin sections cut from a frozen liver may be examined in serum or vitreous humour, but in my experience the method has not been successful.

Hardening may also be effected by placing small pieces in syrup for some weeks, or in dilute alcohol to which a few drops of solution of soda have been added. Of the value of this last mixture I cannot speak too highly. No mode of preparation has afforded more satisfactory specimens, not only of the liver, but of many other tissues. The advantage of this solution seems to depend upon the opposite action of the two fluids. The alcohol tends to precipitate albuminous compounds, and render them hard and more or less opaque. The soda, on the other hand, alone would soften and dissolve them, and make them very transparent. In conjunction, these liquids operate in rendering the tissue hard and transparent at the same time. Large preparations have been preserved in a weak alcoholic solution of soda with advantage. A preparation of the fœtus, about the fourteenth week, prepared in this way, will show very clearly the points of ossification of all the bones ("Microscope in Medicine," Fourth Edition, p. 48, Pl. V). All the textures are perfectly transparent, while the calcareous matter remains opaque. In this manner portions of liver may be made perfectly hard, and at the same time very transparent. A thin section is to be made with a very sharp thin knife, then slightly washed and examined in dilute alcohol or, after soaking for a time, in glycerine. In many of the sections thus prepared, the appearances represented in some of the drawings in the present volume were obtained (Figs. 66, 67, Pl. XX). The same success is, however, by no means always met with, although precisely the same method has been pursued, and it is necessary to examine

numerous specimens of livers of different animals treated in different ways.

Some preparations have been obtained from the livers of animals in which the duct had been tied some hours before death with the view of causing the minute ducts to be distended with bile; and others have been taken from organs of animals during hybernation, when probably no bile had been formed for some time, and into the duct of which injection had been gradually forced until it would contain no more.

But although, in many instances, I was able to satisfy myself of the truth of the most important points which I have advanced with regard to the arrangement of the minute ducts, a number of preparations failed, and I could not *demonstrate* the arrangement in every liver which I tried. I therefore felt it necessary to try to hit upon new and more certain methods of preparation. The ordinary process of injection I had tried many times and in many ways, and like others before me only succeeded so far as consisted in driving the bile into the small ducts. One could not force the injection far enough. The injection seldom reached the surface of the hepatic cell-containing network, and, in many instances, accumulated at this point, in which cases, the appearance of a duct terminating in a blind extremity was produced.

OF INJECTING THE DUCTS OF THE LIVER AND THE HEPATIC CELL-CONTAINING NETWORK, AND OF PREPARING AND PRESERVING SPECIMENS FOR EXAMINATION WITH HIGH POWERS.

The method of using perfectly limpid injection of Prussian blue has been followed by me since the year 1855. The method of employing a perfectly transparent injection made with glycerine was described in my lectures in 1856, and the composition of the fluid was given in the first edition of "How to Work with the Microscope," 1857. For injecting the ducts of glands I found this fluid invaluable.

The introduction of injection into the hepatic ducts and into vessels by the graduated pressure as of a low column of mercury or water was advocated by MacGillivray and others in preference to using a syringe; the injection makes its way very slowly, but the operation may be kept up continuously for many hours, the pressure being uniform during the whole time. Another very ingenious method of injecting the finest hepatic ducts was adopted by Chrzonszewsky ("Virchow's Archiv," 1866).

Many observers have given the preference to transparent injecting fluids made with gelatin. Beautiful specimens have been prepared in this way in which the supposed bile capillary ducts are most distinctly displayed. Prof. Frey long ago sent me some excellent preparations in which the injection could be seen projecting from the cut edge of the

specimen between two of the cells. Prof. Stewart also showed some of his preparations in which the same fact was demonstrated with perfect distinctness. The general inference from these and similar observations was that the injection passed into excessively minute but veritable intercellular and pericellular ducts. In this opinion I could not concur, for it seemed to me the appearances could be explained by supposing that the injection had passed in intercellular spaces and hardened there. The jelly, I think, contracts a little, and when cells are removed little processes of coloured jelly seem to project from the free edge of the cut specimen. The conclusion I formed was that if more force had been employed the injection would have surrounded the cells instead of passing only into the little irregular channels existing between them.

After trying various plans of injection with varying and not satisfactory results, it occurred to me that if the bile could be forced out of the ducts by injecting water into the portal vessels, not only might the smallest ducts be injected but some of the injection might pass on into the cell-containing network. To my great delight, in the very first liver I injected with water, the gall-bladder filled with bile soon after the injection of the portal vein had been commenced, and bile also escaped from the common duct. After a short time, almost pure water ran out from the duct. The water was allowed to escape from the vessels, and then the liver was placed in cloths to soak up the water with which it was saturated. The duct, after a lapse of a few hours, was injected. I have examined the water which escaped from the duct on several occasions. It always contained a large quantity of cylindrical epithelium; and sometimes circular cells from the small ducts were found; but I have never met with specimens of liver-cells, which is easily accounted for when we consider the small calibre of the smallest ducts.

The injecting media which I first used were the old opaque injections; the freshly prepared chromate of lead, as had been used by Sir William Bowman in his investigations on the kidney, yielded good results. The injecting fluid passed into the ducts very readily and with slight force, and could be seen entering the lobules upon the external surface. It did not appear gradually round the circumference of the lobule, as is the case when the portal vein is injected, but it formed small roundish points, to the unaided eye almost like little extravasations, here and there at the circumference of the lobules; and it then spread for a short distance inwards. Upon examining a small piece with the microscope, the small ducts were well seen, and it was evident that they not only went up to the lobules, but that they penetrated into them.

Transparent Injections.—Although the injection had not extravasated, the outline of the network was not distinct, and upon examining thin sections with a quarter, only a confused appearance was visible, and I was unable to demonstrate the relation of the cells to the ducts and to

the vessels. Before I could hope to make out this point, it was clearly necessary not only to inject the ducts, but to inject them in such a manner that they would bear examination with the higher powers, upwards of two hundred diameters. Camboge, carmine, cochineal, lake, and some other more or less transparent colouring matters were employed, but the injection permeated the delicate membrane of the tubes and the adjacent textures were coloured, so that the nature of the arrangement was not clearly proved. Freshly prepared Prussian blue was tried, and with much better success. Now, however, a new difficulty presented itself. The thinnest section which could be obtained necessarily consisted of several layers of the cell-containing network and capillaries on different planes, and, in consequence of the distension of the former by the injection, the latter could not be clearly distinguished. It then occurred to me to try to inject both the portal vein and the duct; the former with plain size, and the latter with Prussian blue. In a liver prepared in this manner I was fortunate enough to see in several different sections, with a quarter of an inch objective, the blue *transparent* injection in one tube in close juxtaposition to a colourless capillary vessel injected with plain size. By varying the kind of injection, and resorting to many experiments which it would be useless to recount, I gradually arrived at a plan of procedure by which specimens could almost always be obtained which would bear examination with a fifth or even with an eighth of an inch object-glass.

Extravasation into the Lymphatics.—Often when too great force is employed, rupture of the walls of a small duct occurs, and the injection not unfrequently passes into a lymphatic vessel. In this way, as was shown by Kiernan, the abundant plexus of lymphatics in the large portal canals can be injected. In one instance the injection passed into the thoracic duct. A similar result likewise occurred to me in a rabbit. This accidental injection of the lymphatics has been noticed by many. Mascagni long ago showed that when injection was thrown into the ducts it returned colourless by the absorbents. Although the lymphatics are so easily injected, I was not at first successful in my attempts to ascertain how these vessels commenced in the liver. The arrangement of the lymphatics of the liver is described in page 55. See Pl. VIII, p. 56.

Directions for Injecting a Liver so that Thin Sections may be made which can be examined with the Highest Powers.—As some observers have expressed doubts as to the possibility of forcing water through the vessels to the extent advocated in my paper ("Phil. Trans.," 1855) without their rupture, and the destruction of the other structures, I propose to describe the several steps of the process as it has been many times carried out. A pig's liver was operated on, but the plan would be precisely the same in making injections of the liver of another

animal. The facts observed in connection with this operation are of interest on other grounds.

Injection of the Liver with Water.—A large pig's liver within half an hour after its removal from the body of the animal was arranged as follows. A piece of glass tube, the sharp edges of which had been removed, and one end a little enlarged in the blow-pipe flame, was inserted into the *portal vein*. The vessel was tied round the tube with strong thread, all chance of slipping being prevented by the dilated extremity of the tube. Another piece of glass tube about four inches in length was inserted into the *hepatic vein* in the same manner. The liver was placed in a dish, over the edge of which the tube inserted into the hepatic vein was allowed to project, in such a way that fluid flowing from it would be conveniently received in vessels placed beneath the stool upon which the dish was supported. A quantity of water at about the temperature of 100° Fahrenheit was placed in a large vessel about four feet above the liver. The water from this reservoir was conducted to the portal vein by means of a glass syphon and india-rubber tube provided with a stop-cock. Before connecting the flexible tube with the portal vein, some of the water was allowed to flow freely through it, and permitted to gravitate into the vein in such a manner as to allow all the air contained in that vessel to rise to the orifice of the tube before the connection was rendered complete. It is very necessary to prevent air from being driven into the capillaries; for if this should happen, rupture of the vessels and extravasation of the fluid will inevitably occur.

The liver having been kept warm by the application of cloths dipped in hot water, the stop-cock was turned so as to allow the water at 100° gradually to pass along the branches of the portal vein, and traverse the capillaries of the lobules. We invariably notice that the entire organ soon swells to twice its size, while blood slowly trickles from the tube inserted into the hepatic vein. The blood soon becomes pale in consequence of its dilution with the water, the liver becomes tense, and the whole surface moist in consequence of the transudation of a little water; the small arteries are distended, the lymphatics are gorged, and the areolar tissue surrounding the vessels in the transverse fissure becomes puffy from the accumulation of water; bile and water pass along the duct and the gall-bladder becomes filled. Its contents may be forced out through the common duct by pressure. It soon becomes refilled, and this process may be repeated many times, the fluid which is removed containing less bile each succeeding time.

The water was allowed thus to wash out the vessels of the liver, and to permeate the ducts, for about four hours, and the fluid collected from the hepatic vein amounted to three hundred and forty-four ounces. The last portions which passed through were perfectly colourless, and

contained no traces of sugar, which substance had been previously detected in considerable quantity. The liver was then removed, and injecting pipes inserted into a branch of each of the following vessels distributed to different lobes :—*portal vein*, *hepatic vein*, *hepatic artery*, and *duct*. A pipe should also be inserted into the branch of *portal vein*, distributed to the lobe in which the duct is to be injected. While the vessels are thus distended with water branches are readily found, and the pipes can be inserted with ease. The liver was then wrapped up in soft cloths, small pieces of sponge being placed here and there, and subjected to considerable pressure, by being placed beneath a board loaded with about fifteen pounds. As the cloths become sodden, they were replaced by fresh ones. The removal of the water in this way will be completed in about twenty-four hours, when the liver will appear shrivelled and of a clayey consistence, and much reduced in size.

It is desirable only to attempt the injection of the liver during cold weather, otherwise decomposition may have commenced before the water has been sufficiently absorbed to admit the introduction of the injection into the vessels. The latter are now quite empty, and ready to receive any injection which the observer may desire to introduce. Some of the Prussian blue injection, p. 217, was carefully forced into the several vessels from a small half-ounce injection syringe, and the process was continued until the masses of liver were properly injected. It is desirable not to push the injection too far, as more is often to be learned from a partial injection than from one in which all the capillaries are completely filled. We have, then, one lobe in which the *portal vein* is injected, another lobe injected from the *hepatic vein*, a third from the *artery*, and a fourth in which the injection has been forced into *the duct*. Of the three former, thin sections may be made after the lapse of a quarter of an hour, with a sharp double-edged scalpel. These may be gently washed on both surfaces, and immersed in weak glycerine consisting of one part water and two parts glycerine. After soaking in this fluid for half an hour, or longer, they may be placed in a cell and examined.

Before, however, the arrangement of the duct can be made out, a further operation is necessary. The injection forced into the duct will pass to the smallest branches, through which it will be conducted to the cell-containing network of the lobule. It will run amongst the cells and distend the tubes of this network to such an extent that adjacent tubes will come into close contact,—the capillary, which intervenes between them, being empty, or nearly so. If a section were made, and examined, we should be able to make out nothing very definite; the duct could be traced into the lobule, and shown to be continuous with the injected portion, but the individual tubular ramifications of the duct and of the cell-containing network could not be made out, or at least only one or two here and there would be demonstrated. It is

obvious that, if the capillaries were injected after the duct, this difficulty would cease, and individual tubes of the cell-containing network would be separated by an injected capillary vessel. The lobe in which the duct has been injected is therefore to be placed in water slightly warm, and the portal vein injected with perfectly clear parchment size. A pipe has already been inserted into this vessel. When the capillaries are quite filled, the pipe is closed with a cork, and the lobe placed in cold water until the size has completely set. A mixture of size and glycerine is better than plain size. When size runs out at the hepatic vein, the open end of the latter may be tied, and a little more carefully injected into the portal vessels, in order to distend the capillary plexus. Lastly, a little size is injected into the duct, in order to distend the larger ducts, and to prevent the injection from returning after it has been forced into the smaller branches. When the liver appears filled, it may be placed in cold water until the size sets.

Thin sections may now be made in any direction, and, as the lobe is very transparent, a small branch of the duct may often be followed for a very considerable distance. The sections should be preserved in glycerine. By comparing specimens from the different lobes which have been injected, the peculiar arrangement, mode of division and distribution of each vessel may be readily made out. With the aid of a neutral tint glass reflector, the outlines of the vessels and duct were traced on paper. The drawings thus made were transferred to stone and printed. "Archives of Medicine," 1857, Pls. I, II, III, IV.

By varying the plan above described somewhat, the different vessels may be injected with different colours. I have succeeded in injecting a human liver with four colours, two being opaque and two transparent. The portal vein was injected with flake white, the artery with vermilion, the hepatic vein with lake, and the duct with Prussian blue. From this liver I have obtained specimens which show very clearly many of the points which have been described. As would be supposed, it was difficult to find a part in which all the vessels and ducts were equally well injected, but here and there small pieces could be found. The figures represented in Pl. I, p. 38, have been copied from sections obtained from this liver.

Carmine Fluid, for Staining all Forms of Bioplasm by Soaking or by Injection—

Good carmine, 10 grains.
Strong liquor ammoniæ, $\frac{1}{2}$ drachm.
Strong glycerine, 2 ounces.
Distilled water, 2 ounces.
Alcohol, $\frac{1}{2}$ ounce.

The carmine in small fragments is to be placed in a test tube, and the ammonia added to it. By agitation, and with the aid of the heat of

a spirit-lamp, the carmine is soon dissolved. The ammoniacal solution is to be boiled for a few seconds and then allowed to cool. After the lapse of an hour, much of the excess of ammonia will have escaped. The glycerine and water may then be added, and the whole passed through a filter or allowed to stand for some time, and the perfectly clear supernatant fluid poured off and kept for use. The solution will keep for months, but sometimes a little carmine is deposited, owing to the escape of ammonia, in which case one or two drops of liquor ammoniæ may be added to the four ounces of carmine solution.

When the vessels are injected with the Prussian blue fluid before the staining process is adopted, the carmine fluid should be sufficiently alkaline to neutralise the free acid present. The permeating power of the solution is easily increased by the addition of a little more water and alcohol. In some cases the fluid must be diluted with water, alcohol, or glycerine, and the observer must not hastily condemn the process or conclude, as some have done, that some particular forms of bioplasm are not to be coloured. Those who speak thus have not given the plan a fair trial, and probably have not tried the effects of a solution containing a little alcohol or otherwise modified.

Notwithstanding the advantages of the above plan and its success in the hands of many observers, objections have been urged against it by some who, I venture to think, have not made themselves familiar with the practical details of the method. It has been said that the formed material may be stained as well as the bioplasm. As every one knows, almost anything may be stained. Hair, horn, wool, paper, &c., may be deeply dyed, even after they have been thoroughly dried. The important fact, however, is not that the tissue may be stained, but that the bioplasm of a tissue *may be deeply coloured, although the formed material which must be traversed by the staining fluid in the first instance is not stained at all.* This is the case of all bioplasm, and it seems to me a fact of far higher significance than is generally admitted. By the process of investigation described it becomes possible not only to distinguish bioplasm in all cases, but to show definitely the mode of formation of the tissue. And in many instances, by this method of proceeding, we can accurately determine which is the *oldest* and which the *youngest* portion of the tissue. In the case of morbid growths, we can demonstrate the part in which growth is going on most quickly, and can distinguish between quickly and slowly growing structure.

Some direct that, when a tissue is too deeply stained, it should be washed in water or in spirit. Such a suggestion could not be made by any one who was aware of the change induced by this colouring process, when properly conducted, or who had seen preparations properly coloured.

The Injecting Fluid.—The following mixture has succeeded admir-

ably in my hands, and I therefore strongly recommend it. It penetrates to the finest vessels and ducts, and into the most minute channels in tissues. It may even be forced into developing capillaries which are only pervious in a part of their course, and into a fine duct up to the point where any temporary or permanent obstruction exists. The fluid never forms a deposit. The specimens injected with it retain their colour perfectly, and the injected tissues can also be stained with carmine.

Pure glycerine, 2 oz. by measure.
Tincture or solution of perchloride of iron, 10 drops.
Ferrocyanide of potassium, 3 grains.
Strong hydrochloric acid, 3 drops.
Water, 1 oz.

Mix the tincture of iron with one ounce of the glycerine; and the ferrocyanide of potassium, first dissolved in a little water, with the other ounce. The Tinctura Ferri Perchloridi and the Liquor Ferri Perchloridi of the British Pharmacopœia since 1867 are of the same strength, and consist of one part of strong liquor ferri perchlor. to three parts by measure of spirit or water. The solutions are to be mixed together very gradually in a bottle, and are to be well shaken during admixture. *The iron solution must be added to that of the ferrocyanide of potassium.* Lastly, the water and hydrochloric acid are to be added. Two drachms of alcohol in the above mixture is of advantage if the capillary walls are very thin, and especially in warm weather.

Preparation of Specimens previous to Examination in the Microscope.—When the ducts and portal vein have been successfully injected in the manner described, the greatest care is requisite in preparing the section for examination. In the process recommended the tissues cannot be hardened for the purpose of cutting thin sections. In the investigation of a solid soft tissue like the liver, no hardening process is likely to yield demonstrative specimens. One does not want a very thin section. A moderately thick one that can be easily frayed out, or even slightly torn, is better, so that a rather long portion of a duct, instead of a mere section of it, can be placed on the slide, and its course and sub-divisions followed for some distance. A very sharp knife, in good order, may be employed. The thin section chosen, after very careful washing, must be placed in a drop of syrup, or glycerine, and the glass cover so applied as to press very slightly upon the specimen. If the washing be not carefully conducted, the superficial cells will be removed, and the vessels will collapse. On the other hand, if all the cells and *débris* adhering to the surface of the section are not washed off with the glycerine, the preparation will appear confused and indefinite. The sections should bear examination with a quarter or eighth of an inch object-glass.

It is, of course, very difficult, and, in great measure, a matter of chance, to obtain a section including a considerable portion of the course of a very small duct, and it will often be necessary to examine very many sections before a demonstrative specimen can be obtained. When we consider how difficult it is to obtain a section of the mammalian kidney, showing, even for a short distance, the convolutions of a single uriniferous tube, it need not excite surprise that it is rare to obtain a section of the liver which shows clearly the termination of the smallest branches of the duct, for these tubes in passing only a very short distance often occupy very many different planes. The circumstances which render the demonstration of the course of the uriniferous tube very difficult operate still more forcibly in the case of the liver, as the tubes are very much smaller, the tissue of which they are composed more delicate, and the entire organ so soft that very slight manipulation is sufficient entirely to destroy the relative positions of the anatomical elements of which it is composed.

We may often succeed in obtaining beautiful specimens of injected ducts by removing portions of the ligamentous extensions from the edge and sides of the liver, which are very valuable for demonstration. Kiernan has given a very correct figure of some of these anastomosing ducts, which I have had copied in Fig. 36, Pl. XI. In some of the small animals—rabbit, rat, guinea-pig—I have succeeded in obtaining specimens of this kind in which a few lobules appeared as it were flattened out. In these the distribution of the finest branches of the duct was well seen. So also demonstrative specimens may often be obtained by shaving off thin slices close to large branches of the portal vein which had been previously injected with plain size, and allowed to cool. The walls of the portal vein in the smaller rodents are so beautifully thin that good specimens of the finest branches of the duct may sometimes be obtained by carefully removing a section of the vein, and spreading it out upon the glass slide, Pl. XV.

Specimens of Diseased Liver and Morbid Growths.—Satisfactory preparations may sometimes be made as follows :—An artery large enough to receive a fine injecting pipe is found, the pipe inserted and properly tied in. Then some of the carmine fluid is carefully injected (a syringe of not more than half an ounce capacity being used, and care being taken that it is thoroughly clean and in good order) until the part supplied by the branch of artery is of a bright red colour. Next a little glycerine and water (two parts of glycerine and one of water) is gently injected for the purpose of washing away the carmine fluid in the pipe and branch of the artery. The whole is then left in a cool place for from twelve to twenty-four hours, the latter not being too long if the weather is cool. The blue injecting fluid is then introduced with great care, and with the least possible pressure. The redness gradually gives

place to a blue tint. When this decidedly predominates the injection is complete. All superfluous tissue may then be removed, and the piece which is most thoroughly injected transferred to a small clean vessel that can be covered over to exclude dust, and glycerine containing one-third part of distilled water added so as to nearly immerse the specimen. After twelve hours' soaking, the greater part of the glycerine, now coloured and containing *débris*, may be poured away, and a little strong glycerine containing ten drops of acetic acid to the ounce added. This process is repeated day by day until the piece of tissue regains its blue colour. Sections may now be cut with a very sharp thin knife, and transferred to a little of the glycerine and acetic acid placed in a watch-glass. After having soaked for some time, they may be submitted to examination, and may be preserved in strong glycerine containing not more than five drops of strong acetic acid to the ounce. It will be observed that in this method of preparation the tissue is in contact with fluids miscible with water from first to last. Some degree of hardening is produced, and this may be increased by adding to the glycerine a little chromic acid and bichromate of potash solution, as described in "How to Work with the Microscope," but one cannot obtain thin sections of considerable area as by the hardening processes at present popular. These, however, produce such changes, and by their use so many structural points I can show clearly enough by other methods may be altogether lost, that I cannot accept some of the appearances seen in the specimens as representing the real structure of the part. In delicate nerve-tissues especially are these processes defective, and lead to a very erroneous idea of structural arrangement. The liquid filtering through the vascular or duct walls from the injecting fluid I have recommended preserves the tissue, and only requires the addition of a little more strong glycerine to the preparation to preserve it permanently. The process, at least in my own hands, worked admirably, and by its employment I have been enable to prepare very thin specimens of the most delicate textures, particularly of the ultimate distribution of nerve-fibres in the smaller vertebrata, which showed more than I was able to demonstrate by any other process. The preparations had also the great advantage of enabling me to demonstrate the disposition of nearly all the component textures in a single specimen. Great care is requisite for the successful preservation of specimens prepared as I have described, and which have to be preserved in strong glycerine, but the observer is well repaid for the extra trouble. As regards permanency, I have many specimens which have retained their characters for more than thirty-five years, but still they cannot be regarded as permanent as specimens which can be preserved in Canada balsam and such media.

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